Pain following spinal cord injury

Thesis

Presented to the Faculty of Arts of the University of Zurich

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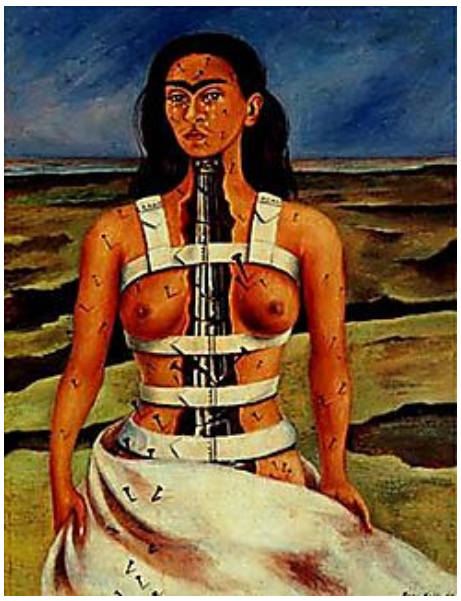

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Preface

"Pain is whatever the experiencing person says it is, existing whenever he says it does" (McCaffery).

Pain is a highly subjective experience and perception; additionally it is a multidimensional phenomenon unfolding itself in various aspects and types. To combine this heterogeneity in an objective, standardized assessment tool was a challenging issue. Moreover, to learn that one can suffer from pain in body areas which are anesthetic due to nerve damage was an enriching experience.

Picture on front page:
Broken column – Frieda Kahlo

My special thanks goes to the University hospital of Balgrist, Zurich, Switzerland where this thesis was carried out. I gratefully acknowledge the generous financial support of the International Foundation for Research in Paraplegia (IFP; Zürich, Switzerland) as well the International Spinal Research Trust (ISRT, London, UK), which made this research possible.

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Finally, I would like to dedicate this thesis to my beloved boy friend; Ulrich Mehnert without him this thesis (in particular in the last few weeks) would not have been possible!

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ABSTRACT

Abstract in English

The present thesis addressed the development of pain in SCI patients and its impact on functionality in daily living in acute SCI patients.

Pain was surveyed with the newly developed Pain-Report within the framework of the European Multicenter study for human Spinal Cord Injury (EM-SCI). The three studies investigated the following aspects of pain in SCI. (1) The design of a SCI-specific survey and its application in a cross section design in a sub acute sample (2) The incidence and time course of main pain types was investigated as well as the shift between pain types within the sub-acute phase (3) The influence of pain and depression on the functional outcome within first 12 months. The results of the first study revealed that the Pain-Report is a feasible tool to survey pain after SCI. It further enables to classify pain according to the IASP (2001) with a high interrater-reliability. The second study points out the importance of classifying into pain types since they showed a different incidence as well as time course. Moreover, it could be demonstrated that once pain is manifested the likelihood for persistence is high e.g. 78% SCI patients initially experiencing neuropathic pain did also at 6 months post injury. The results of the third study revealed that within the first 6 months neither pain nor depression had a significant influence on the functional outcome. However, one year post injury depression showed an effect on functionality.

These results are discussed in the context of present literature. Concluding, the findings are highly relevant for clinic as well as for research, as they provide important knowledge about development of pain after SCI.

Abstract in deutsch

Die gegenwärtige Dissertation beschäftigt sich mit der Entwicklung von Schmerzen bei Querschnittpatienten und deren Beeinträchtigung auf die Funktionalität im Alltag. Die Schmerzen wurden mit dem neu entwickelten Pain-Report erfasst und im Rahmen der Multizentrischen Studie für Querschnittpatienten (EM-SCI) durchgeführt. Die drei Studien untersuchten folgende Aspekte von Schmerzen nach einer Querschnittlähmung. (1) Die Entwicklung eines für Querschnittpatienten spezifischen Interviews und dessen Anwendung in einer Querschnittstudie. (2) Die Inzidenz and der zeitliche Verlauf der drei Hauptschmerztypen und deren Wechsel zwischen einander während der subakuten Phase. (3) Der Einfluss von Schmerz und Depression auf die Funktionalität im Alltag während des ersten Jahres. Die Resultate der ersten Studie zeigen, dass der Pain-Report ein praktikables und anwenderfreundliches Messinstrument ist, um Schmerzen nach einer Querschnittlähmung zu erfassen. Des Weiteren ermöglicht der Pain-Report die Schmerzklassifizierung nach IASP (2001) mit einer hohe Interrater-Reliabilität. Die Resultate der zweiten Studie unterstreichen die Wichtigkeit einer Klassifizierung in Schmerztypen, da diese sowohl eine unterschiedliche Inzidenz als auch einen anderen Verlauf aufzeigten. Weiterhin konnte darauf Aufmerksam gemacht werden, dass eine hohe Wahrscheinlichkeit für ein Andauern von Schmerzmanifestation besteht, da in 78% von den Patienten, die initial neuropathischen Schmerz hatten, dies auch nach 6 Monaten der Fall war. Die dritte Studie ergab, dass während den ersten 6 Monaten weder Schmerzen noch eine Depression einen signifikanten Einfluss auf die Funktionalität haben. Nach einem Jahr jedoch zeigte das Vorhandensein einer Depression einen Effekt.

Diese Resultate werden im Anschluss im Kontext mit der gegenwärtigen Literatur diskutiert. Die Befunde konnten zu einem profunderen Wissen über die Entwicklung von Schmerz nach einer Querschnittlähmung beitragen und sind von grosser Relevanz sowohl für die Klinik als auch für die Forschung.

1. Introduction and background

This thesis is based on three studies (submitted papers) which are topically connected and in a hierarchically order. Study 1 aimed to design a SCI-specific standardized pain interview (named the Pain-Report), study 2 focuses on the incidence and course of the different pain types within the first 6 months, and study 3 investigated the influence of pain and depression on the functional outcome. In the following, a brief theoretical introduction into the topic "Pain following spinal cord injury" is presented, including an annotation about what a SCI is and subsequently a disquisition about pain, where the most important facts concerning pain are summarized. As depression is strongly related to pain a summary is presented at the end of chapter 1. In part 3 are the main results illustrated in original articles. Subsequently, the results are discussed in context with literature.

All three studies were conducted within the framework of The European Multicenter Study for Human Spinal Cord Injury (EM-SCI; www.emsci.org). This network was established with the purpose of having standardized examinations and its results should provide a basis for future therapeutic interventions (Curt et al., 2004). At the moment, a total of 19 paraplegic centers build up a close collaboration to discuss, plan and realize prospective studies. In total over 1600 patients (May, 2009) with spinal cord injury are included in the EMSCI database. Patients with acute traumatic spinal cord injury are tested and documented within a fixed time schedule at the following five stages: stage 1 within the first 15 days post injury, stage 2 at one month (16-40 days), stage 3 at three months (70-98 days), stage 4 at six months (150-186 days) and stage 5 at twelve months (300-400 days). The collected data from each centre are sent to the coordinating centre (Zurich) in regularly time intervals to be joined into a central database.

The complexity of the individual SCI requires a holistic examination as requested in the EM-SCI guidelines. The neurological examination is performed according to the protocol of the American Spinal Cord Injury Association (ASIA, 2002) (for explanations see chapter 1.2.1). Further neurophysiological assessments consist of somatosensory

and motor evoked potentials, as well as nerve conduction velocity testing. Functional tests include the Spinal Cord Independence Measure (SCIM; Catz et al., 1997; Catz et al., 2001; Catz et al., 2007) to assess independence and activities of daily life. The walking capacity is measured by The Walking Index for Spinal Cord Injury (WISCII II; Ditunno et al., 2000) and the timed 10m walking tests (van Hedel et al., 2005). In the EM-SCI, assessors receive regularly an ASIA training (twice per year; once in German and once in English), to improve the skills for the assessment and classification of the neurological impairment; although the classification is also performed by a computer algorithm (see also Spiess et al., 2009).

1.1. State of knowledge in pain following SCI

In the past decades pain following SCI reached an increasing attention and is presently established as common sequela of SCI. Obviously, the history of SCI pain is not that old yet but consists of manifold - partly resolved - issues. Fortunately, the understanding of pain following SCI and partly its underlying mechanisms is progressed in the last years. Scientific findings resulted in identifying various changes in the nervous system responsible for pain development. Last but not least, one of the most important issues: an approach to a consensus in pain classification could be reached by agreeing on pain terminology (the one from the IASP). This, in turn, led to a better communication among clinicians and researchers working in the field of pain.

The prevalence of SCI pain is rated of around 69% (Bonica, 1991; Stormer et al., 1997; Siddall et al., 1999, Dokladal et al. 2009). Patients rate experiencing pain following SCI as one of their major problems (Rose et al., 1988; Widerstrom-Noga et al., 2001). Chronic pain is even superimposed on the limitations caused by their injury (Widerstrom-Noga et al., 2007) and once a person develops pain, it is unlikely that the pain problem resolve on its own (Ehde et al., 2003). For the majority experiencing pain can become life-long experience that can progressively worsen over time. At present, there is no adequate therapy available what means that patients have to cope with that problem in their own way.

SCI patients experiencing pain are more likely to experience psychological distress such as depression or anxiety (Kennedy and Rogers, 2000b). Compared to patients without pain they have reduced leisure time activities (Murphy and Reid, 2001; Ravenscroft et al., 2000), as well as lower employment rates (Ravenscroft et al., 2000; Rintala et al., 1998). Pain could interfere with sleep (Norrbrink Budh et al., 2005; Widerstrom-Noga et al., 2001), and sexuality (Westgren and Levi, 1998) and might have a negative influence on the individual's rehabilitation outcome (Siddall, 2009). Summarized, experiencing chronic pain might result in reduced quality of life (QoL) and in impaired health (Lundqvist et al., 1991; Westgren and Levi, 1998; Putzke et al., 2001; Murphy and Reid, 2001; Putzke et al., 2002a).

Several methodological limitations did hamper communication between researchers and clinicians in the field of SCI: i) the lack of consensus in terminology, ii) lack of consensus in pain classification, iii) few studies which investigated pain prospectively

in the acute phase after SCI. These discrepancies might have partly contributed to the wide disparity in the prevalence rate since there are findings ranging from 18% to 96% (Anson and Shepherd, 1996; Demirel et al., 1998; Siddall et al., 1999; Hicken et al., 2002; Putzke et al., 2002a). Additionally, the wide disparity can be attributed to no-existence of a SCI specific assessment tool. To address these shortcomings was the aim of this thesis.

1.2. Spinal cord injury

A Spinal Cord Injury (SCI) is an injury to the spinal cord (including cauda equina) that results in loss of motor, sensory, and / or autonomic function, which is manifested in the following sequelae of SCI like dysfunction of the bowel and bladder (including infections of the bladder and anal incontinence), sexual dysfunction, spasticity, autonomic dysreflexia, muscle atrophy, osteoporosis, disabilities to breath (if the injury is cervical), and pain. The consequences are either temporary or permanent.
Before World War II, the life expectancy of a spinal cord injured person was estimated in months (Summers et al., 1991). Within the last decades medical technology did progressed and SCI patients are able to survive close to a normal life span, if the acute stage remains without any life-threatening circumstances (Crook et al., 1986). Despite this positive change in life extension, negative side effects, complications and difficulties including chronic pain might still occur following SCI. A person with SCI may experience pain long after the fracture or damage of bones and nervous tissues is healed.
A SCI can occur through different mechanisms but the three leading common causes of SCI are: Destruction from direct trauma, compression by bone fragments, hematoma, or disk material and ischemia from damage or impingement on the spinal arteries (edema occurs subsequently to any of the SCI's causing further damage).
The most common cause of spinal cord injury is trauma. Nearly half of the injuries are caused by motor vehicle accidents. Other types of trauma include: falls from heights, sporting injuries (diving, football, biking, equestrian, etc.), and violence (stabbing or gunshot wounds to the spine). Spinal cord injury can also be caused by compression of

the cord by a tumor, infection, or inflammation. Some patients have a smaller than normal spinal canal (called spinal stenosis) and are at a higher risk of injury to the spinal cord.

The incidence in Switzerland is 50-60 SCI subjects per 1 million inhabitants; this rate is similar to other industrial countries (Ackery et al., 2004; Dryden et al., 2003; Martins et al., 1998; O'Connor, 2002; Pickett et al., 2003). In the member states of the Council of Europe are estimated 300 000 people living with SCI (2003) and about 11'000 new cases every year (Finnerup and Jensen, 2004). However, it should be considered that most studies capture solely traumatic SCI subjects.

1.2.1. Classification of spinal cord injury

Since the classification of SCI is part of the used pain classification it will be discussed in detail.

A SCI is mainly classified by two factors: level and completeness of lesion (Figure 1 and 2). The first factor is divided in tetraplegia (replaced the term quadriplegia) and paraplegia. Tetraplegia refers to impairment or loss of motor/sensory function in the cervical segments of the spinal cord due to damage of neural elements within the spinal canal. Tetraplegia results in impairment of function in the arms as well as in the trunk, legs and pelvic organs. It does not include brachial plexus or injury to peripheral nerves outside the neural canal (ASIA, 2002). While paraplegia refers to impairment or loss of motor and/or sensory function in the thoracic, lumbar or sacral (but not cervical) segments of the spinal cord, secondary to damage of neural elements within the spinal canal. With paraplegia, arm functioning is spared, but, depending on the level of injury, the trunk, legs and pelvic organs may be involved. The term is used in referring to cauda equine and conus medullaris injuries, but not to lumbosacral plexus lesions or injury to peripheral nerves outside the neural canal (ASIA, 2002). With the ASIA classification system, the terms paraparesis and quadriparesis now have become obsolete.

Completeness of lesion is defined as the absence of sensory and motor functions in the lowest sacral segments (i.e. complete) whereas incomplete is defined as the preservation of sensory or motor function below the level of injury, including the lowest sacral segments (ASIA, 2002).

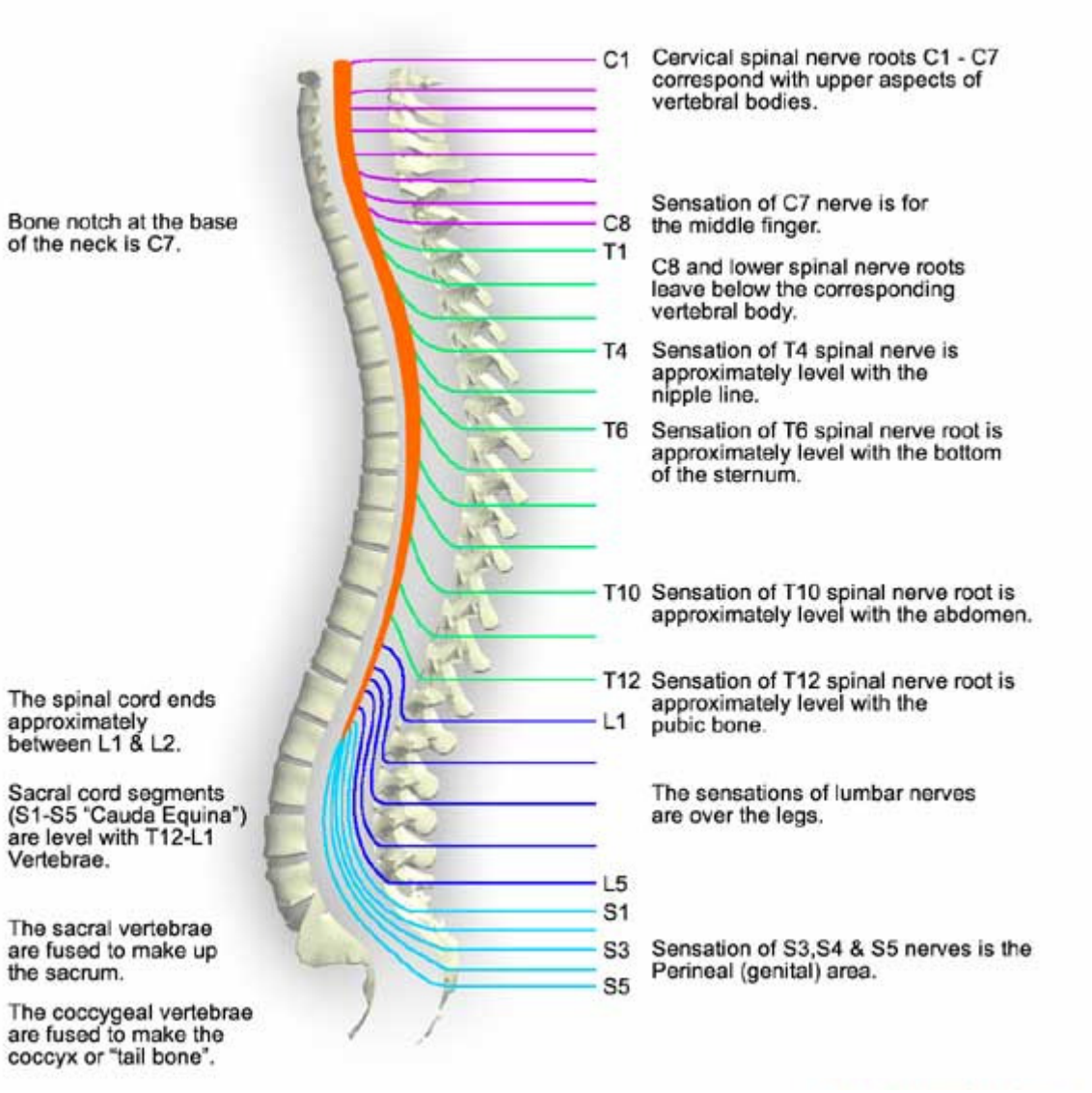


Figure 1: Diagram showing the relationship between spinal nerve roots and vertebrae.

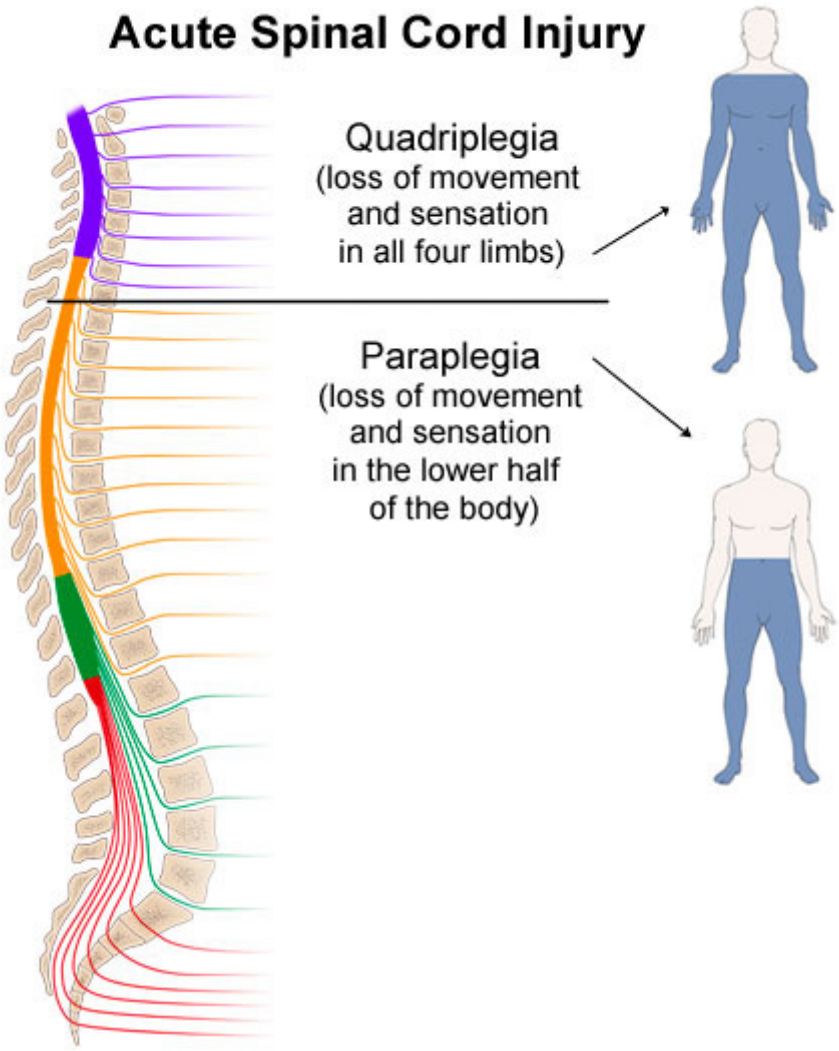


Figure 2: Illustration of terminology and the affected limbs.

Both factors defining a SCI are investigated by using a standardized protocol (Figure 3) of the American Spinal Injury Association (ASIA). A trained assessor measures motor (motor score) as well sensory function (light touch; pin prick) in each segment.

The neurological examination has sensory and motor components, which are tested separately. The sensory examination is completed through testing of a key point in each of the 28 dermatomes (right and the left side of the body) (Austin, 1972). Two aspects of sensation are examined at each of these key points: sensitivity to pin prick (usually tested with a disposable safety pin) and to light touch (tested with cotton swab) (Bracken et al., 1990); both are rated and scored on a three-point scale: 0 = absent, 1 = impaired (partial or altered appreciation, including hyperesthesia), 2 = normal, NT = not testable

The motor examination is completed through the testing of a key muscle (right and left side of the body) in the 10 paired myotomes *(collection of muscle fibers innervated by the motor axons within each segmental nerve (root)).* The strength of each muscle is graded on a six-point scale (ranging from 0 = total paralysis to 5 = normal active movement, full range of motion against full resistance) (ASIA, 2002).

Sacral-sparing is evidence of the physiologic continuity of spinal cord long tract fibers with the sacral fibers located more at the periphery of the cord. Indication of the presence of sacral fibers is of significance in defining the completeness of the injury and the potential for some motor recovery.

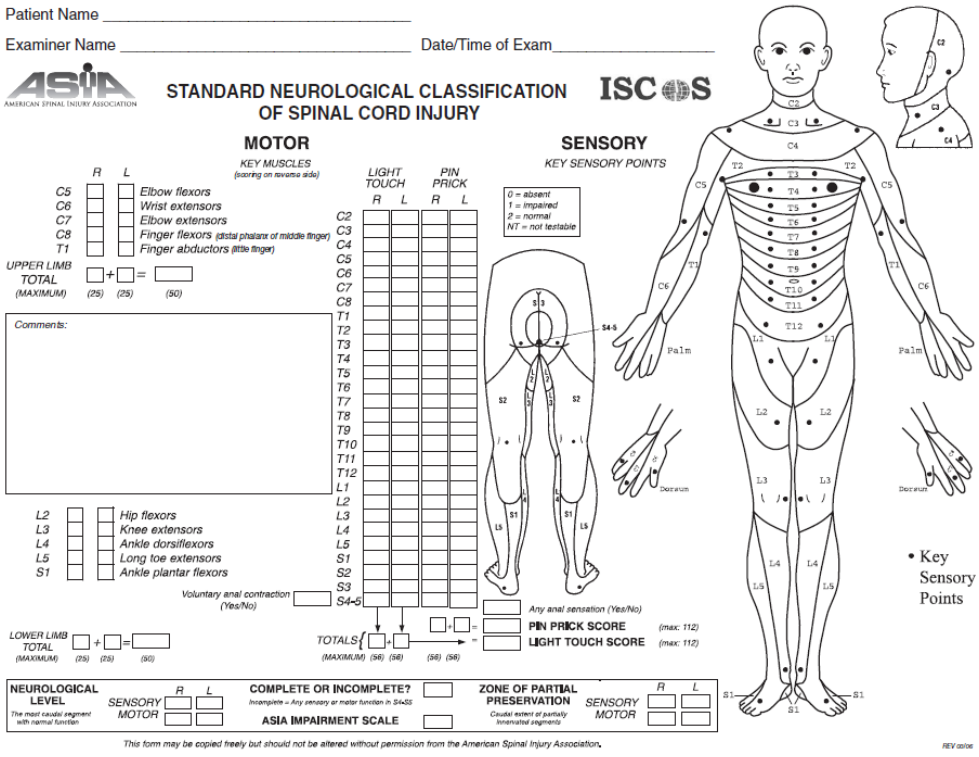


Figure 3: Standardized protocol for measuring neurological function (e.g. motor and sensory function) in patients with SCI (ASIA, 2002).

Table 1: Displayed are the ASIA impairment scale and the meaning of the classification letters.

A - Complete:	No sensory or motor function is preserved in sacral segments S4-S5.
B - Incomplete:	Sensory, but not motor, function is preserved below the neurologic level and extends through sacral segments S4-S5.
C - Incomplete:	Motor function is preserved below the neurologic level, and most key muscles below the neurologic level have muscle grade less than 3.
D - Incomplete:	Motor function is preserved below the neurologic level, and most key muscles below the neurologic level have muscle grade greater than or equal to 3.
E - Normal:	Sensory and motor functions are normal.

The ASIA classification using the description of the neurological level of injury is now the standard in terminology and is used to classify types of SCI (e.g. C8 ASIA A with zone of partial preservation of pinprick to T2).

1.3. Pain in SCI

1.3.1. Parenthesis: Pain in general

Pain, in the sense of physical pain, is a sensory experience that may be described as an unpleasant awareness of a noxious stimulus. Pain is part of the body's defense system, triggering a reflex reaction to retract from a painful stimulus, and helps adjust behavior to increase avoidance of that particular harmful situation in the future.
But pain is not a single entity; rather it is a set of various components. Several areas in the brain need to be activated that an individual can perceive pain, areas which are not solely pain specific. Moreover, pain is also a product of a psychological state, a mental

experience and consciousness. The subjective experience of pain consists of the followed components (Mense, 2004): The sensory-discriminative component which allows identification of the pain stimulus (type, localization, intensity, duration), the emotional-affective component which is responsible that pain hurts, leads to avoidance in future similar situations, the vegetative-autonomic component that leads to an increase in blood pressure or sweating, the motor component reflecting motor reflexes or pain utterances, and the cognitive component which results of a conscious appraisal of the others components. Areas involved in pain processing as described above are displayed in Figure 4.

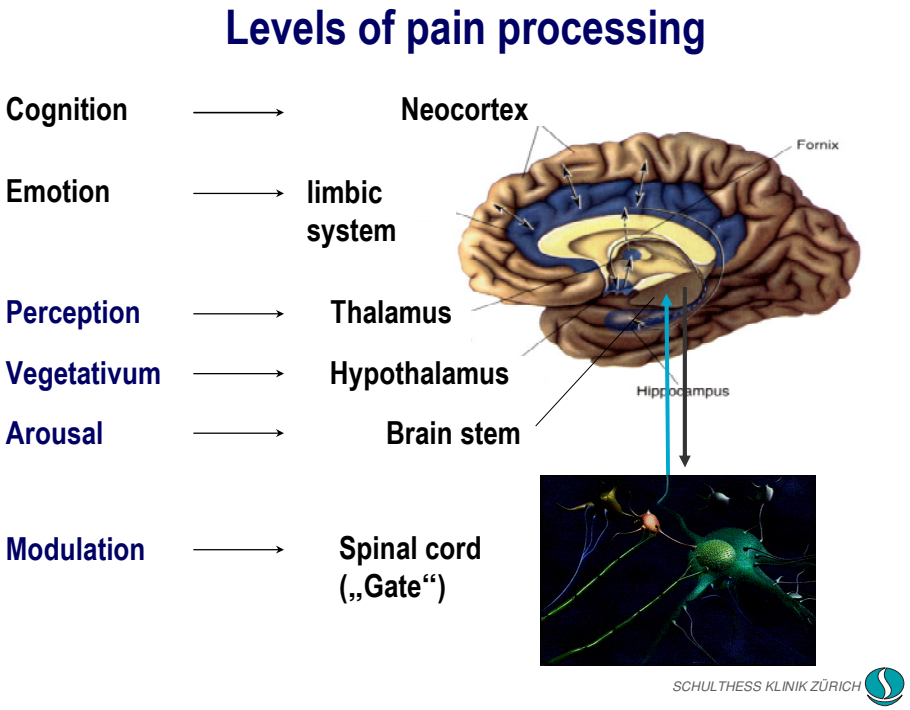


Figure 4: Brain areas, which are involved in pain processing (in agreeableness of the Schulthess Klinik).

The described heterogeneity in pain indicates that a unicausal, only somatic pain concept can not meet these requirements. Therefore pain is considered as a multicausal accumulative psychophysical experience and is termed as a bio-psychosocial phenomenon.

Given its significance, physical pain is also linked to various cultural, religious, philosophical, or social issues.

For scientific and clinical purposes, pain is defined by the International Association for the Study of Pain (IASP; formed almost 30 years ago, is a nonprofit, interdisciplinary organization devoted to understanding the mechanisms of pain and improving the care of patients with pain through research, education, and communication) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage"

The definition emphasize that pain is a multidimensional problem. Further, it demonstrates that pain, beside the fact that it is a sensation, is always subjective and unpleasant and therefore an emotional experience.

"Activity induced in the nociceptor and nociceptive pathways by a noxious stimulus is not pain, which is always a psychological state, even though we may well appreciate that pain most often has a proximate physical cause" (Widerstroem-Noga).

Pain in SCI

Although the loss of motor, sensory, and / or autonomic functions are the most debilitating consequences after SCI chronic pain is often reported as being one of the most displeasing phenomena following SCI (Rose et al., 1988; Widerstrom-Noga et al., 2001). Both acute and chronic pain can occur in SCI. Underlying differences are listed in table 2.

Table 2: Differences between acute and chronic pain.

Acute pain	**Chronic pain**
< 3 months duration	> 3 months duration
Protective, preventing further damage	Prevents normal function
Useful	Not useful

Simply, acute pain can be defined as pain that occurs immediately after acute injury or a disease. While chronic pain persists beyond the duration of injury or disease. Understandable, that acute pain can progress into chronic pain state since a huge nociceptive input can, through toxic effects of excitatory amino acids, permanently change spinal-cord function, and therefore, lead to chronic pain after an acute injury

(Eldabe and Raghaven, 2008). Developing risk factors for chronic pain and long-term disability have been well researched and identified particularly for acute low back pain. These risk factors (Table 3) are termed as psychosocial barriers to recovery (Cavill, 2008).

Table 3: Psychosocial barriers to recovery (Cavill, 2008).

Belief that pain and activity are harmful	Problems and / or dissatisfaction at work
Sickness behaviors such as extended rest	Problems with claims or compensation or time off work
Social withdrawal	Overprotective family; lack of support
Emotional problems such as low or negative mood, depression, anxiety or stress	Inappropriate expectations of treatment

It is reported that similar factors are also related to the development of chronicity for other pain conditions (Cavill, 2008). Moreover, it is suggested that psychosocial factors are more important than medical factors in the development of chronicity (Cavill, 2008). Nevertheless, this concept of the development of chronic pain is valid for nociceptive pain e.g. low back pain. But to what extent these factors might be associated with the development of chronic neuropathic pain remains unanswered.

After SCI, both **nociceptive** and **neuropathic pain** can develop. To differentiate between these two pain types is crucial as the underlying mechanisms and their perception are different and they also demand specific treatments.

Nociceptive pain results from activation of peripheral nociceptors due to ongoing tissue damage. Peripheral nociceptors are high threshold free nerve endings stimulated by high intensity stimuli, including mechanical, thermal or chemical stimuli (Meyer et al., 1994; Eide, 1998). This kind of pain may be induced by damage of skeletal structures and ligaments in the spine, as well as overuse of muscles, and decubitus causing injury of skin and muscles. An important distinction compared to neuropathic pain is that common analgesics like non-steroidal anti-inflammatory drugs (NSAIDs), and general treatments like physical therapy, are in most cases effective. There are two subtypes of nociceptive pain, namely musculoskeletal and visceral pain.

Musculoskeletal pain refers to pain occurring in regions of normal sensation. Therefore pain could be localized above, at and below level of lesion. This kind of pain is mostly described such as dull or aching, related to movement and is clearly localized; i.e. pain presentation and pathology are consistent. Responsiveness to pharmaceutics is high.
Examples of causation: mechanical pain, spinal fractures, muscular injury, shoulder overuse syndromes and muscle spasms (Donovan et al., 1982; Siddall and Loeser, 2001; Cardenas et al., 2002; Bryce et al., 2006).
Visceral pain originates from the body's viscera (*organs in the cavity in the body*), visceral nociceptors are located within body organs and internal cavities.
Following SCI visceral pain has usually a delayed onset and is mostly described as burning, cramping and constant but fluctuating pain in the abdomen. It may be due to normal afferent input via sympathetic or vagal nerves in paraplegics and via vagus in tetraplegics (Siddall et al., 2002). A relationship to visceral pathology or dysfunction like infection or constipation is mostly present (Donovan et al., 1982; Siddall and Loeser, 2001; Bryce et al., 2006; Cardenas et al., 2002).
Examples of causation: Urinary tract infection, uretretic calculus and bowel impaction.
The differentiation between visceral and neuropathic pain is not always clear.
The most challenging pain type is the neuropathic pain type (Synonyms: Deafferentiation pain, diffuse pain, central pain, dysaesthetic pain syndrome, phantom sensations, phantom body pain, neurogenic pain, neurologic pain, spinal cord injury pain).is defined as *being caused by a lesion or dysfunction of the nervous system* (IASP).
The neuropathic pain syndrome is characterised by loss of sensory modalities mediated by spinothalamic tract neurones, and abnormal pain perception (spontaneous continuous and abnormal evoked pain). Peripheral neuropathic pain is caused by damage of peripheral nerves or nerve roots, while central neuropathic pain depends on damage within the central nervous system.
Mostly, described as: **burning**, **tingling**, **stabbing** and **electrifying**. Usually, reported as a constant pain and unrelated to position or activity, but may worsen with infections and may be triggered by sudden noises or jarring movements (Siddall et al., 2002). It appears to be the most common pain following SCI and the most difficult to treat since this type of pain may be often resistant to pharmaceutics.
SCI neuropathic pain is divided according to the level of injury: consequently termed as above, at- and below level pain: i) **above level pain** includes pain that is not specific to

SCI i.e. compressive mononeuropathies and complex regional pain syndrome (CRPS I and II). SCI people may be more susceptible because of wheelchair use and transfers compared to the general population. In particular SCI patients with cervical lesions are at higher risk of developing CRPS in the upper limbs (Siddall et al., 2002), ii) **at-level pain** can occur at the border of normal sensation and anesthetic skin and is defined as that it occurs within a band of two or four segments and can be unilateral or bilateral and circumferential. Onset of developing is usually within the first few months after injury, iii) **below level pain** is perceived in anesthetic regions, mostly bilateral and therefore characterized as below-level pain.

1.3.2. History of pain and pain mechanisms

Going back to the 17th century the concept about pain was coined by René Descartes. He hypothesized that pain was transmitted from the periphery along specific pain fibres up to the brain where a specific pain region was activated.

Figure 5: Descartes illustration about the body / mind split concept.

His "mind/body split" concept of pain was valid until the middle of the twentieth century (Siddall, 2009). More, this statement had an impact until these days in relation to pain following SCI.

In 1965, another theory arose that had a major impact on our understanding about pain (Melzack and Wall, 1965). The concept, known as the gate theory, proposed that the perception of physical pain is not a direct result of activation of nociceptors, but instead is modulated by interaction between different neurons, both pain-transmitting and non-pain-transmitting. The theory asserts that activation of nerves that do not transmit pain signals can interfere with signals from pain fibers and inhibit an individual's perception of pain.

Some people could not believe that SCI patients are capable to experience pain since their transmission of sensation along "wires" is cut. Now, we know that this misconception of the nervous system as a passive transmitter of sensory information is

false. In fact, many SCI patients develop pain due to their transsection of the spinal cord nerves (Siddall, 2009).

In relation to pain following SCI still several problems are unresolved since "there is a set of observations on pain in paraplegics that just does not fit the theory" (Melzack, 1991). This put out the challenge to find a new pain concept that is not only about pain modification of peripheral inputs but for pain that is present despite of the loss of peripheral inputs (Siddall, 2009). With this challenging issue we are standing at the present time and at the very beginning about understanding of underlying mechanisms of pain following SCI.

The abnormal paradoxon of (painful) sensory deficits which are experienced in regions of loss of afferent sensory function is probably the most important characteristics of neuropathic pain (Table 5). Allodynia and hyperalgesia are considered to be two characteristic features of central neuropathic pain while paresthesia and dysesthesia are considered to manifest due to peripheral neuropathic pain.

Table 4: The most common neuropathic pain characteristics and their definitions.

Characteristics of neuropathic pain	**Definition**
Allodynia	Evocation of pain by non-noxious stimuli.
Thermal	Cold and warm stimuli evoke sensation of pain.
Tactile	Light touch can be experienced as painful.
mechanical	Touch or pressure can be experienced as painful
Hyperalgesia	An increased response to noxious stimuli due to a lowered threshold.
Static	Gentle pressure on skin evokes pain.
Punctuate	Stimuli such as pinprick are painful.
Dynamic	Light brush evokes pain sensations.
Paraesthesia	An **abnormal but non-painful sensation**, which can be spontaneous or evoked. (Often described as pins and needles or tingly and are assumed to reflect spontaneous bursts of activity in A-Beta fibres.)
Dysesthesia	An **abnormal unpleasant but not necessary painful sensation**, which can be evoked spontaneously or by external stimuli. (Probably due to sensitization of C-nociceptors.)

In addition to the most common characteristics, a variety of further characteristics exist, which are summarized in: Eide, 1998; Jensen et al., 2001; Finnerup et al., 2003).

However, little is known about developing factors of neuropathic pain; the present knowledge is summarized subsequently. Sensory loss and abnormal pain perception are probably one of the most prominent characteristics of neuropathic pain. These patho-physiological conditions (caused by injury or dysfunction of the nervous system) might lead to excitability in nerve fibres for mechanic, thermal and chemical stimuli. This emerged ectopic excitability can lead to abnormal perception (i.e. paresthesia) and pain.
In healthy, the different sensory modalities are usually mediated to the brain via different sensory afferent neurons and processed central neuronal pathways (Willis and Coggeshall, 1991). Sensations of temperature and pain are signalled via thin myelinated/unmyelinated A-delta/C fibres, second order projecting neurones in the spinal cord dorsal horn ascending in the spinothalamic pathways, and third order thalamic neurones projecting to the cerebral cortex (Eide, 1998). Sensations of vibration, joint position as well light touch/pressure are signalled via thick, myelinated sensory neurons, second order neurones ascending in the dorsal column, and third order thalamic neurones ascending to the cerebral cortex (Eide, 1998). Abnormal pain perception includes three different components: a) spontaneous continuous pain usually burning and aching quality, b) spontaneous intermittent pain usually stinging quality and c) abnormally evoked pain usually produced by touch or movement.
Stimulus-evoked pain may be abnormal leading to allodynia, hyperalgesia or hyperpathia. Abnormal up-regulation of neuronal activity may play a key role in the development of abnormal pain perception. Deafferentation may cause abnormal changes in the firing pattern of neurones signaling pain sensation. This includes following mechanisms as suggested by electrophysiological studies (Eide, 1998): increased spontaneous activity, reduced thresholds and increased responsiveness to peripheral stimulation, and expansion of the peripheral receptive fields of central neurons.
Impaired sensation of temperature can be determined by a quantitative thermotest (suggesting damage of A-delta / C fibres) and impaired light touch can be determined by so called pinprick or light touch test (suggesting damage of thick myelinated fibres or dorsal column).

1.3.2. History of classification

Numerous definitions and categorizations of pain were published in the last decades, mostly causing confusion and making clinical application difficult. Several categorization schemes have been proposed based on etiological and descriptive approaches: The etiological approach focuses on physiological or physical mechanisms that cause the pain. In contrast, the descriptive systems focus on pain factors including location, duration of pain, time of onset, verbal descriptors and pain aggravating and alleviating factors. Etiological information is also included but seems not crucial for the classification. The etiological approach would be more appropriate but is too expensive and time consuming. Therefore, descriptive approaches are more often used as they are cost-effective.

One of the earliest and simplest categorization divided pain into above-, at-, and below level pain (Michaelis, 1970). This scheme distinguished itself through simplicity but implicated numerous limitations as it did not address pathology or it was not useful when patients had an incomplete SCI.

A broad overview is reported in Hicken et al. (2002) who reviewed SCI pain classification systems in the literature over the last 50 years and found a range of 2-15 subtypes of pain per scheme (Hicken et al., 2002; Bryce et al., 2006). However, to discuss all these schemes here in detail would reach beyond the thematically focus of this thesis. A more comprised and latest review was done by (Sawatzky et al., 2008) who reviewed articles published between 1986 and 2006 and identified 5 SCI pain classification systems (which are listed in Table 3).

Table 5: Overview of reviewed classifications and their psychometric properties (Sawatzky et al., 2008).

	Measurement properties		
Instrument	*Number of studies*	*Reliability (intra/inter)*	*Convergent validity*
Classification measures			
Donovan pain classification	1	++/+++	0
Tunks pain classification	2	+/++	0
Siddall (IASP Task Force)	1	++	0
Bryce/Ragnarsson taxonomy	1	++	0
Cardenas pain classification	1	++	0
Pain perception measures			
Graded Chronic Pain Disability Scale (GCP)	2	+++	++
Multidimensional Pain Inventory–Spinal Cord Injury (MPI-SCI)	1	++/+++	++
McGill Pain Questionnaire (MPQ)	1	++	++
Medical outcomes survey (SF-36)	1	0	++
Pain interference measures			
Wheelchair users Pain index (WUSPI)	2	++/+++	++
Brief pain inventory (BPI)	2	+++	+++

+++, excellent evidence; ++, adequate evidence; +, poor evidence; 0, no numerical evidence.

Early concepts of classifications like those from Tunks (1986), or (Donovan et al., 1982) were adjuvant by providing rudimentary categorizations for SCI pain. During decades this process went on and more specific classification systems could have been developed. Including the generally agreement that a taxonomy which is divided into tiers provides a structure that may aid clinical assessment, identification of mechanisms and treatment. However, to improve communication in the field of SCI pain a uniform classification is needed. Hence, the latest three classification systems are illustrated: The latest SCI pain categorization **Cardenas' Chronic Pain Classification System** consists of two major categories, i.e. neurologic (neuropathic) and musculoskeletal pain and is constructed as a multi-axial assessment protocol. Other criteria are level of lesion, level of pain (e.g. at-, below and above lesion), pain laterality, responsiveness to pain stimuli / activity and SCI completeness (Cardenas et al., 2002). The neuropathic pain is further divided into: SCI pain (below level of lesion, in an area without normal sensation), transition zone (occurs at the level of the lesion), radicular (may occur at any dermatomal level, usually unilateral and radiates, and is related to activity and position), visceral pain (felt in the abdomen, not related to activity, affected by position or associated with allodynia). The musculoskeletal pain is divided into: mechanical spine pain (pain in the back or neck affected by activity and position), overuse pain (often above injury level in areas of normal sensation or sometimes below level, if the injury is incomplete).

The **Bryce / Ragnarsson-SCI-Pain-Taxonomy** is constructed as a three tier decision tree schema (Table 4). Pain is classified by level of injury, pain type (nociceptive or neuropathic elements) and subtype (regional localization) (Bryce et al., 2006). In tier 1 pain is localized according to the level of lesion (i.e. above, at-, or below level), tier 2 identifies pain as nociceptive or neuropathic and in tier 3 pain is categorized into subtypes according to region. This schema is very similar to the one of Siddall's.

Table 6: Illustration of Bryce/Ragnarsson pain taxonomy.

Location		Type	Etiologic Subtype
above level	nociceptive	1	mechanical/musculoskeletal
		2	autonomic dysreflexia headache
		3	other
	neuropathic	4	compressive neuropathy
		5	other
at level	nociceptive	6	mechanical/musculoskeletal
		7	visceral
	neuropathic	8	central
		9	radicular
		10	compressive neuropathy
		11	complex regional pain syndrome
below level	nociceptive	12	mechanical/musculoskeletal
		13	visceral
	neuropathic	14	central
		15	other

The most known and used classification is the one modified from Siddall's initial construction and later introduced by the IASP Task Force on Pain following SCI (Siddall et al., 2000). Since this classification was used also in our studies (which are part of this thesis) it will be discussed in more detail. The IASP classification uses three tiers (Table 7):

Table 7: Showing the three tiers taxonomy according to IASP, 2002.

Broad Type (Tier 1)	Broad System (Tier 2)	Specific Structures/Pathology (Tier 3)
Nociceptive	Musculoskeletal	Bone, joint, muscle trauma or inflammation. Mechanical instability. Muscle spasm. Secondary overuse syndromes
	Visceral	Renal calculus, bowel, sphincter dysfunction, etc. Dysreflexic headache
Neuropathic	Above level	Compressive mononeuropathies. Complex regional pain syndromes
	At level	Nerve root compression (including cauda equina) Syringomyelia Spinal cord trauma/ischaemia (transitional zone, etc.) Dual level cord and root trauma (double lesion syndrome)
	Below level	Spinal cord trauma/ischemia (central dysesthesia syndrome, etc.)

The first tier divides pain very broadly into nociceptive and neuropathic types and provides a general direction. The differentiation is based on the presumed location and patient's descriptors. While the second tier provides further definition of these broad pain types and offers further direction for treatment. Nociceptive pain is categorized into musculoskeletal and visceral pain, while neuropathic pain is divided according to the level of lesion, e.g. above-, at-, and below level. The third tier provides a specific structure and pathology and might identify more detailed a possible mechanism.

An important argument for choosing the IASP taxonomy in our study was the fact of its use in two longitudinal studies (e.g. 6 months and 5 years) conducted by Siddall et al. (2003; 1999). There the classification was performed primarily according to pain location and descriptors.

The 6-month-follow-up study (Siddall et al., 1999) was the first prospective, longitudinal study that has investigated time of onset, prevalence, and severity of specific pain types in 100 SCI patients from initially 2 weeks up at several time points (i.e. 8, 13, and 26 weeks) within the first 6 months. The subsequent study was

performed 5 years later with the same sample. Follow up data from 73 patients (73%) was obtained.

Table 8: Prevalence rates of the two longitudinal studies (Siddall et al., 1999; 2003).
Pain prevalence according to time stage post SCI:

	2 weeks	**6 months**	**5 years**
Pain in general	91%	64%	81%
Musculoskeletal	65%	40%	59%
Visceral	< 5%	< 5%	< 5%
Neuropathic at-level	38%	36%	41%
Neuropathic below level	14%	19%	34%

The time of onset for each type of pain varied. Different pain types demonstrated also different time courses within in 6 months. Fifty-three percent of patients experiencing at-level pain showed an onset at 2 weeks whereas the onset of below level pain was in 51% within 2 or more years post injury. The onset of musculoskeletal pain was in 46% within the first 3 months.

Within 6 months post injury one third (21%) rated their pain as severe. At 5 years the rate even increased up to 53% (5% rated their pain as excruciating).

Physical factors associated with SCI showed correlations between level of lesion and prevalence of pain, e.g. pain was significantly higher in those with thoracic level (92%), allodynia was higher in those with cervical SCI (39%) than those with thoracic lesions (8%) and the prevalence of allodynia was significantly higher in those with incomplete injuries (33%) compared to complete injuries (11%). Concerning completeness and overall prevalence of pain no significant results could have been found. Five years later no relation between overall pain and injury level or completeness could have been shown.

Both studies demonstrated the importance of differentiating between pain types since they showed different time of onset and courses and have not been replicated before our studies, so far.

Further, during the period of conducting our studies the decision to use this classification system has been confirmed by several pain committees like the National Institute on Disability and Rehabilitation Research (NIDRR) spinal cord injury measures meeting (Bryce et al., 2007) and the Spinal Cord Outcomes Partnership

Endeavor (SCOPE; Alexander et al., 2009) published recommendations for assessments in SCI by proposing the IASP taxonomy. The IASP classification was also used by the Pain Data Set (Widerstrom-Noga et al., 2008) a recently published questionnaire developed specifically for pain in SCI.

1.4. Depression in SCI

Furthermore, pain can have a significant influence on mood, leading to depression and even to suicide (Rintala et al., 1998; Segatore, 1994; Westgren and Levi, 1998), for review see (Craig et al., 2009). During rehabilitation the attention of therapists and patients is predominantly focused on physical factors, while psychological and social factors are being addressed later.

A spinal cord injury (SCI) is a decisive event in life, which demands a long lasting process in acceptance and adjustment. The following disturbances like loss of mobility, sensitivity and vital functions (e.g. impairment in bladder and bowel or sexual functions) can restrict social life and cause psychological distress (Siddall et al., 2002). Therefore, the appearance of depression after SCI can not be neglected and will be discussed.

For a long time it was asserted that a depression was an inevitable reaction to SCI (Dryden et al., 2005). Researchers suggested that patients must develop a reactive depression following SCI to achieve a healthy adjustment. If the patient has not shown depressive symptoms it was considered as patients' denial (Kennedy and Rogers, 2000b). Later, stage models of adjustment to SCI were proposed and depression was always integrated. It was proposed that SCI patients pass through several temporal sequences and one of them is a phase of depression. However, little empirical validation supported the existence of these stages. Contemporary it seems to be established that experiencing a depression following SCI depends on personality, individual coping strategies and personal resources, and is not a necessary part of the process of adjustment to SCI (Dryden et al., 2005).

The depression rate in general population is reported between 4 and 10% (Dryden et al., 2005). The prevalence of depression among newly injured SCI patients is ranging from 20% to 43% (Fullerton et al., 1981; Frank et al., 1985; Judd et al., 1989; Kishi et al.,

1995; Kennedy and Rogers, 2000b; Dryden et al., 2005) compared to a community based sample varying between 11% and 60% (Barrett et al., 2003; Hancock et al., 1993; Craig et al., 1994; Scivoletto et al., 1997; Kennedy and Rogers, 2000; Bombardier et al., 2004; Craig et al., 2009). However, here again a lack of consensus in terminology and consequently in diagnosis of depression might have partly contributed to this variability in the prevalence rate.

One can assume that approximately 30% suffer a depression following SCI in the acute stage as well in a community-based sample (Craig et al., 2009).

These data indicate that only a significant minority of SCI patients tend to develop depressive symptoms and the majority (at least 50%) do not develop any psychological morbidity (e.g. anxiety disorder, post-traumatic stress disorder, alcohol abuse) following SCI (Craig et al., 2009). Furthermore, the prevalence of depression (20-43%) in SCI patients during the rehabilitation process is consistent with any other patient group being hospitalized because of other illnesses or injuries (Craig et al., 2009).

Research involving depression following SCI has been limited by two primary factors. First, there is a wide variability in the definition of the term depression. While some refer to a depression meaning despondency and grief following SCI, others define depression according to DSM-IV or ICD-10. According to (Elliott and Frank, 1996) *the differentiation between depressed mood or affect refers to a state of dysphoria that occurs routinely and is a normal process. Whereas depressed mood accompanied by persistent and pervasive loss of emotional involvement with other people, objects, or activities distinguishes a normal mood state of sadness, demoralization, or other negative affects such as anxiety from the syndrome of depression.* Diagnosis of depression is presently sill depending on the attending physician and that might be without training in the area of psychiatry.

Second, few studies have examined depression prospectively in a longitudinal study (Elliott and Frank, 1996). Thus, a retrospective bias remains and conclusions are difficult to draw.

Diagnostic criteria for mental disorders are descriptions of symptoms that can be clustered in four categories: i) affective or mood symptoms include depressed mood and feelings of worthlessness or guilt, ii) behavioral symptoms include social withdrawal and agitation, iii) cognitive symptoms, or problems in thinking include difficulty with concentration or making decisions and iv) somatic or physical symptoms include insomnia or hypersomnia.

According to the Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV) depression is defined as following:

Diagnosis of Major Depressive Disorder, Single Episode

A. The person experiences a single major depressive episode:

1. For a major depressive episode a person must have experienced at least five of the nine symptoms below for the same two weeks or more, for most of the time almost every day, and this is a change from his/her prior level of functioning. One of the symptoms must be either (a) depressed mood, or (b) loss of interest.

a. Depressed mood.

b. Significantly reduced level of interest or pleasure in most or all activities.

c. A considerable loss or gain of weight (e.g., 5% or more change of weight in a month when not dieting). This may also be an increase or decrease in appetite. For children, they may not gain an expected amount of weight.

d. Insomnia or hypersomnia.

e. Behavior that is agitated or slowed down. Others should be able to observe this.

f. Feeling fatigued, or diminished energy.

g. Thoughts of worthlessness or extreme guilt (not about being ill).

h. Ability to think, concentrate, or make decisions is reduced.

i. Frequent thoughts of death or suicide (with or without a specific plan), or attempt of suicide.

2. The persons' symptoms do not indicate a mixed episode.

3. The person's symptoms are a cause of great distress or difficulty in functioning at home, work, or other important areas.

4. The person's symptoms are not caused by substance use (e.g., alcohol, drugs, medication), or a medical disorder.

5. The person's symptoms are not due to normal grief or bereavement over the death of a loved one, they continue for more than two months, or they include great difficulty in functioning, frequent thoughts of worthlessness, thoughts of

suicide, symptoms that are psychotic, or behavior that is slowed down (psychomotor retardation).

B. Another disorder does not better explain the major depressive episode.

C. The person has never had a manic, mixed, or a hypomanic Episode

The diagnosis of mood disorder due to a general medical condition is:

A. A person has significant disturbance in mood that includes either (or both):
   1. Depressed mood or significantly reduced level of interest or pleasure in most or all activities.
   2. Mood that is euphoric, heightened, or irritable

A. The person's symptoms are directly related to the presence of medical condition.

B. Another disorder does not better explain the mood disturbance.

C. The mood condition is not present only when a person is delirious.

D. The symptoms are a cause of great distress or difficulty in functioning at home, work, or important areas.

Although, research involving depression following SCI has been limited as reported above and adequately to pain research no specific depression assessment tool for SCI patients exists at present the BDI has been proven useful in the SCI population, as shown in several studies (Craig et al., 2009; Craig et al., 1994; Hancock et al., 1993; Kennedy and Rogers, 2000b; Malec and Neimeyer, 1983; Richards, 1986).

Derived from the clinical observations the Beck Depression Inventory (BDI) was first published in 1961 (Beck et al., 1961). The BDI is a self-administered instrument and takes generally 5-10 minutes to complete. It consists of 21 symptoms and attitudes which can be rated from 0 to 3. The items were chosen to assess the intensity of depression and were not selected to reflect a particular theory of depression.

The 21 symptoms and attitudes are: Mood, pessimism, sense of failure, lack of satisfaction, guilt feelings, and sense of punishment, self-dislike, self-accusation, suicidal wishes, crying, irritability, social withdrawal, indecisiveness, and distortion of body image, work inhibition, sleep disturbance, fatigability, and loss of appetite, weight loss, somatic preoccupation and loss of libido.

A total score can be calculated by summing up the individual scores of the 21 items. Cut-off scores were made to determine the severity of the depression (Table 9).

Table 9: Defined cut-off scores.

< 10	None or minimal depression
10-18	Mild to moderate depression
19-29	moderate to severe depression
30-63	severe depression

The BDI is one of the most commonly used tools for assessing depressive symptoms (Bombardier et al., 2004) and has been proven useful in the SCI population, as shown in several studies (Malec and Neimeyer, 1983; Richards, 1986; Hancock et al., 1993; Craig et al., 1994; Kennedy and Rogers, 2000b; Craig et al., 2009).

2. Aims of the studies

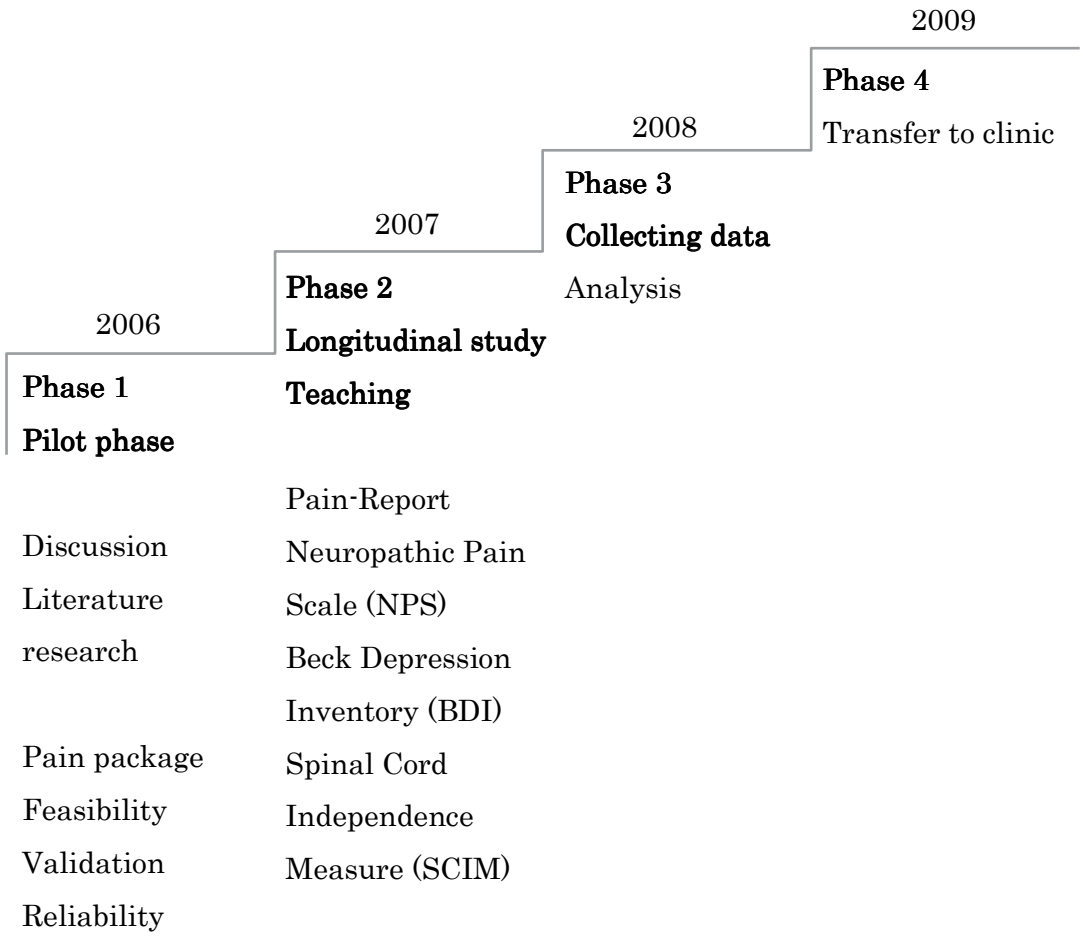
The aims of the studies underlying this thesis were

1) the design of a pain screening tool specifically for SCI patients (phase1)

2) to assess the incidence and time course of the common main pain types following SCI (phase 2, 3)

3) to examine the influence of pain and depression on daily activities (phase 2, 3)

Table 10: Illustrates the relation between the three experimental studies conducted in my thesis.



The specific goals of Studies1-3 were:

Study 1. A screening tool for pain and pain related factors specifically for subjects with spinal cord injury

The aim of the first study was to develop and test a screening tool for pain after spinal cord injury (SCI) suitable for use in clinical and experimental settings. This newly developed Pain-Report, conceived as a structured interview, examines various aspects of pain and should help to better classify SCI pain according to the guidelines of the International Association for the Study of Pain (IASP, 2001).

Previous limitations:

Present pain questionnaires showed limitations for our purpose. First, they were neither specifically designed for SCI patients nor practicable in a clinical setting. Second, common pain questionnaires did not allow a classification of pain types as advised by the IASP. The resulting variability in pain anamnesis, mostly dependent on a particular physician, enhanced the difficulties to compare existing results. Finally, most assessments are time consuming and not feasible in the daily clinical routine.

Hypothesis:

Based on its structure the Pain-Report will be simple and short in application. In combination with neurological and medical information, the Pain-Report will provide sufficient information to differentiate between neuropathic and nociceptive pain.

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Study 2. The incidence and course of pain and pain related symptoms within the first six months after SCI (study 2)

Results in Study 1 indicated that the Pain-Report is a practicable tool for assessing pain in SCI patients. The objectives of Study 2 were twofold. First, to detect the incidence of pain following spinal cord injury (SCI) and to prospectively monitor the course of main pain types (e.g. nociceptive and neuropathic pain) at three time points within 6 months post injury. Second, we focused on the nature of pain itself. We first investigated its time course followed by the shifts between pain types within several time points.

Previous limitations:

Several studies investigated incidence and prevalence of pain following SCI with different or even contradictory results. This inconsistency points out various problems. First, the sample of SCI patients was assessed at different and often lengthy times after injury. Second, a retrospective report is not as reliable as a prospective data collection and represents therefore not an accurate reflection of reality. Third, there was no consistency in identifying or classifying pain types.

We, therefore, tried to address these shortcomings by using the Pain-Report combined with the IASP taxonomy and focused on the sub-acute stage, i.e. a prospective, longitudinal assessment at three time points starting at 4 weeks, three and six months following injury.

Additionally, several studies investigated the relation between pain after SCI and physical factors (e.g. completeness of injury, level of injury, age, gender, etc) with inconsistent results. Precise information about development and course of pain (types) with probably predictive value would be very useful, especially, for treatment and in respect of future therapeutic interventions.

Hypothesis:

We hypothesize, based on clinical experience and previous studies that nociceptive pain has a high occurrence initially and decreases during the sub-acute phase, while the development of neuropathic pain progresses with time.

Study 3. Pain and depression hardly affect daily life activities within the first year after spinal cord injury

The goal of study 3 was to investigate whether pain and / or depression have a negative impact on the performance of daily life activities (ADL) within the first year after spinal cord injury (SCI). In addition, we addressed the question whether the objective level of ADL performance corresponds to the perceived level of interference.

Previous limitations:

Literature suggests that pain and depression have a negative impact on the rehabilitation outcome after SCI, although this has not been investigated adequately. Most studies investigated the influence of physical factors (e.g. neurological impairment, disability) and pain on quality by addressing subjective criteria without objective measurements. Second, most studies investigated in community-based samples and did not take into account the mental state of the patient in the rehabilitation setting and right after discharge. And finally, there was a need to investigate the influence of pain and / or depression on the functional outcome within the sub acute phase.

Hypothesis:

We hypothesized to find a confirmation of former results in the literature that pain as well was depression has a negative impact on daily life activities.

Submitted to Pain

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3. OWN CONTRIBUTIONS

3.1. A screening tool for pain and pain related factors specifically for subjects with spinal cord injury (study 1)

Abstract

The objective of the study was to develop and test a screening tool for pain after spinal cord injury (SCI) suitable for use in clinical and experimental settings. This newly developed Pain-Report, conceived as a structured interview, examines various aspects of pain and should help to better classify SCI pain according to the guidelines of the International Association for the Study of Pain (IASP, 2001).

The present study was conducted within the framework of the European Multicentre Study for Human Spinal Cord Injury (EM-SCI) using a cross-sectional design.

Sixty-eight SCI patients with pain were assessed between 1 and 6 months post-injury. The first part of the Pain-Report assessed pain and the second part assessed pain associated factors, general well-being and common sequelae of SCI.

Following results could be revealed: The Pain-Report was simple and fast in application and well accepted by the patients. It collected the most important features of pain and enabled to differentiate between nociceptive and neuropathic pain. The inter-rater reliability of the Pain-Report showed a percentage of agreement of 89% and a Kappa value of 0.79. In the neuropathic pain group, allodynia and paraesthesia was significantly more present and the descriptors burning, hot and tingling more frequent. Although half of the patients described their general well-being was as good, one third showed symptoms of mild depression.

It can be concluded that the Pain-Report is a feasible tool and, in combination with neurological information and the medical history of the patient, can be used to classify pain. It further provides information about the complexity of pain and pain related factors after SCI.

Introduction

The European Multicenter Study for Human Spinal Cord Injury (EM-SCI) network was established with the purpose of having standardized examinations and its results should provide a basis for future therapeutic interventions (Curt et al., 2004). The complexity of the individual SCI requires a holistic examination as requested in the EM-SCI guidelines. The neurological examination is performed according to the protocol of the American Spinal Cord Injury Association. Further neurophysiological assessments consist of somatosensory and motor evoked potentials, as well as nerve conduction velocity testing. Functional tests include the Spinal Cord Independence Measure to assess independence and activities of daily life, as well as walking capacity measures such as the Walking Index for Spinal Cord Injury and timed walking tests (www.emsci.org). All these examinations are conducted within the first year post injury at five fixed time stages.

Beside the apparent consequences after SCI as loss of motor, sensory and autonomic functions, pain is often rated by patients as one of their major problems (Anke et al., 1995). It was therefore consequential to incorporate a pain assessment into the EM-SCI: First to have a long term follow up on pain after SCI to improve pain treatment and second to have a database for novel therapeutically interventions.

To fulfill these requirements we developed a pain screening tool. This Pain-Report was designed specifically for SCI patients and applicable in both clinical and research fields. The tool should give information about pain itself and pain related factors such as mood, anxiety, sleep and daily limitations. Most important, it must assess pain syndromes to finally classify pain types according to the International Association for the Study of Pain (IASP, 2001). Based on this taxonomy, SCI pain can be grouped into a nociceptive and a neuropathic pain type. Within these groups, it can be further divided into subtypes (e.g. musculoskeletal or visceral pain, either at or below the lesion) and finally, into presumed mechanisms (specific structure and pathology).

The present study reports on the development and first evaluation of the Pain-Report and discusses its limitations.

Methods

Subjects

The practicability of the Pain-Report was tested in a cross sectional study in four German and Swiss EM-SCI centers. Sixty-eight SCI patients actually experiencing pain

participated in the structured interviews. Descriptive information on the patient samples are presented in Table 8. Seven of the patients were tested after one month, 29 after 3 months and 32 after six months. The study was approved by the local ethics committees.

Table 11: Patients' demographics

Descriptives	**Numbers**
Gender	
Male	50 (73.5%)
Female	18 (26.5%)
Etiology	
Traumatic	68 (100%)
Injury	
Paraplegic complete	22 (32.4%)
Paraplegic incomplete	17 (25.0%)
Tetraplegic complete	16 (23.5%)
Tetraplegic incomplete	13 (19.1%)
Age [years] (mean ± SD, range)	40 ± 15.96 (15-76)
Time post injury [days] (mean ± SD, range)	109.5 ± 90.85 (14-480)

Construction of the Pain-Report

A preliminary list of items was generated on the basis of research literature (Barrett et al., 2003; Siddall et al., 2002; Siddall et al., 1999) and clinical experience (anamnestic data, medication, location of the pain, pain descriptors, allodynia, paraesthesia, pain intensity, onset, frequency and change over time of pain, alleviating and aggravating factors). A selection of these items was made following discussions with two neurologists and two psychologists, all with expertise in the SCI field, and presented in the form of a structured interview. Further, accordingly to recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT; Dworkin et al., 2005), it was suggested that the combined assessment of pain severity as well as physical and emotional functioning would best capture the multidimensionality of pain (Dworkin et al., 2005). Therefore, coherent pain factors (e.g. mood, anxiety, sleep quality, limitations in daily life) were implemented into the Pain-Report (Hammell, 2007; Norrbrink Budh et al., 2005).

The Pain-Report which contains 23 items (16 defining aspects of pain and 7 coherent pain factors), and is presented in Appendix 1. The original German version was translated by a professional translation agency. Questions 1 to 4 assess information about pain, depression and the use of medication prior to the accident. In question 5 the pain location is drawn on a pictogram (see Fig. 6). If the SCI patient suffers from several pains, questions 6 to 16 have to be answered for the most intensive pain. While question 6 assesses the intensity of several pain descriptors, questions 7 and 8 evaluate the presence and intensity of allodynia and paraesthesia. Question 9 addresses the intensity of pain at the time of the examination, as well as the average and maximum pain intensity during the last week. Questions 10 to 13 record further information about the course of pain over time. Questions 14 to 16 assess accompanying side effects, as well as alleviating and enhancing factors. Questions 17 to 22 address affective factors and finally, question 23 evaluates typical side effects that can occur after SCI. Questions 6 to 16 can be repeated for the second or even third most intensive pain.

Assessment procedure

The first author performed all the structured interviews and timed their duration. After the structured interview, a battery of pain questionnaires was applied, to validate and complement the information of the Pain-Report: the Neuropathic Pain Scale (NPS) (Galer and Jensen, 1997), the Pain Experiencing Scale (SES) (Geissner, 1995) and the

first part of the Multidimensional Pain Inventory (MPI-D) (Kerns and Decker, 1985). Finally, the Hamilton depression Scale (HAMD) was applied (Hamilton, 1967). Subjects unable to complete the questionnaires due to physical disabilities were assisted.

Data Analyses

First, the characteristics of the sample were described for the most intense pain (i.e. Pain 1) and the outcomes of the Pain-Report were quantified for the three patient groups with various times after injury (1, 3 and 6 months).

Second, two experienced psychologists (first and second authors) independently evaluated each Pain-Report. They combined the information obtained from the Pain-Report with the results from the neurological examination, as provided by the EM-SCI database (see introduction), and the medical history to classify pain into nociceptive and neuropathic pain. The reliability was compared between the two raters and the agreement was quantified by the percentage of agreement using the Kappa value (inter-rater reliability). The prevalence of the pain types was reported for each time point.

Third, the patients were grouped into a neuropathic and nociceptive pain group. Differences between these groups were tested for the NPS scores and the affective and sensory part of the SES, using the Mann-Whitney-U test. Similarly, differences in the rating of single items of the SES were determined between the two groups using Chi-square tests or Fisher's exact test.

Fourth, the ratings of single items for affective factors of pain such as general mood and anxiety were quantified and correlated with similar items from the MPI-D using Spearman's correlation coefficient. The data were analyzed using SPSS Version 14.0.2 for Windows. The level of significance was set at 0.05.

Results

The Pain-Report was simple in application, well understood by the patients and this structured interview lasted in general only 10 minutes. Of the 68 SCI patients, 36 suffered from a unique pain, 29 from two pains, and 3 from 3 different pains. The pain locations are presented in Figure 6 and the frequency of common related sequelae of SCI (question 23) are listed in Table 12.

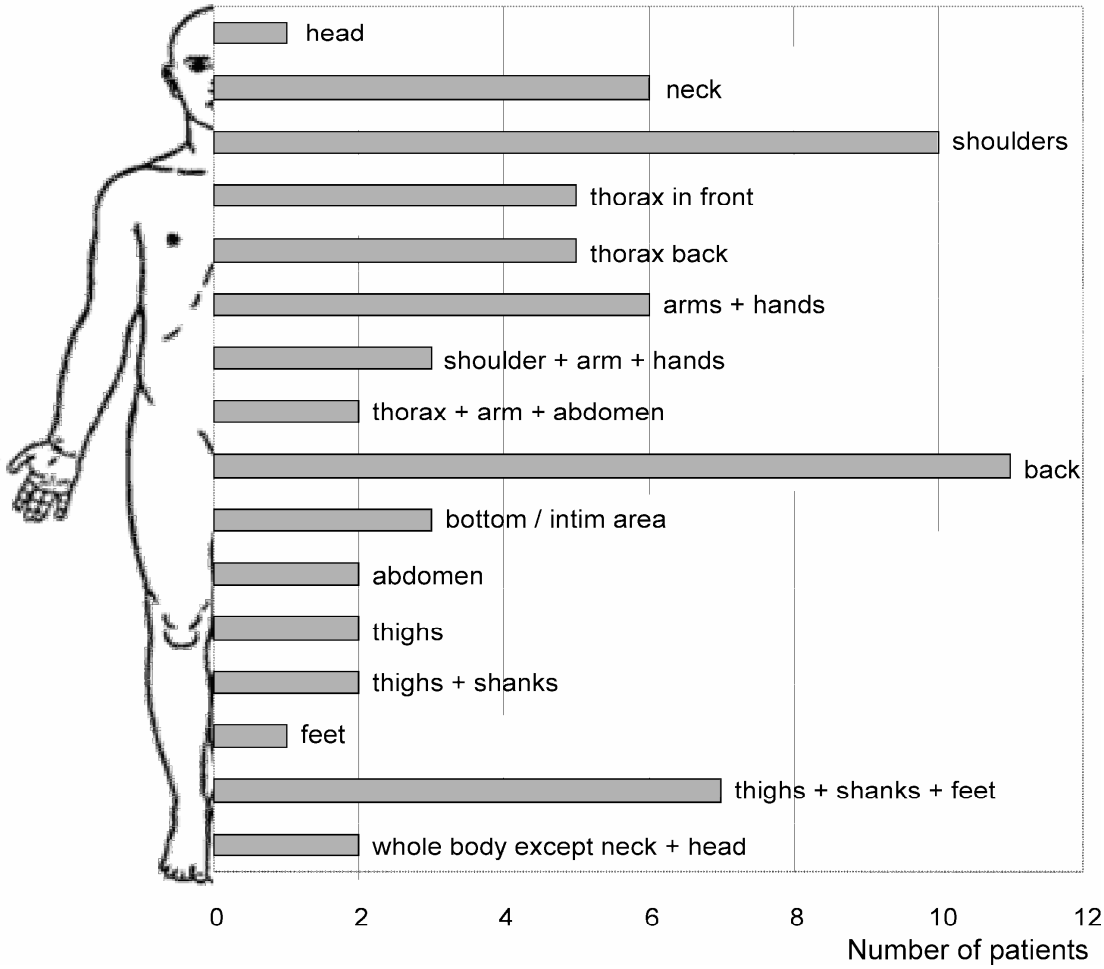

Figure 6: Pictogram adapted from the Pain-Report showing the location of pains on the different body parts. The numbers represent quantity of experienced painful areas; shown only for the first (most severe) pain.

Table 12: Common sequelae of SCI rated on a numeric rating scale.

Physical sequelae of SCI	N of answers	Mean + SD
Decreased mobility	68	8.1 + 2.3
Decreased ability to control bladder	62	7.0 + 3.0
Decreased ability to control bowel function	60	6.7 + 3.1
Pain	68	4.3 + 2.5
Sexual dysfunction	54	4.1+ 3.1
Muscle spasms	48	3.8 + 2.5
Infections	12	5.5 + 3.1
Pressure ulcers	10	5.3 + 3.4

Scores: 0= not at all, 10=very much. Abbreviations: N, number; SD, standard deviation.

Description of pain

Of the 36 subjects who were considered to have nociceptive pain, 34 had musculoskeletal pain and 2 visceral pain. Neuropathic pain was diagnosed in 32 subjects; 12 subjects had at level pain and 20 below level pain.

The inter-rater reliability of the Pain-Report was good with a percentage of agreement of 89% and a Kappa value of 0.79.

The two groups showed no difference in present, average and maximal pain intensity, which was rated on an 11 point NRS-scale (see Table 13). However, allodynia was significantly more frequently reported in the neuropathic group as compared to the nociceptive group (16/32 versus 7/36, respectively; p = 0.003). The same result was found for paraesthesia (14/32 versus 2/36, respectively; p = 0.001). The occurrence of the pain types is presented in Figure 7, which presents the numbers for musculoskeletal and visceral pain separately. Musculoskeletal and neuropathic pains have a similar occurrence, while visceral pain occurred later in this cross-section study design.

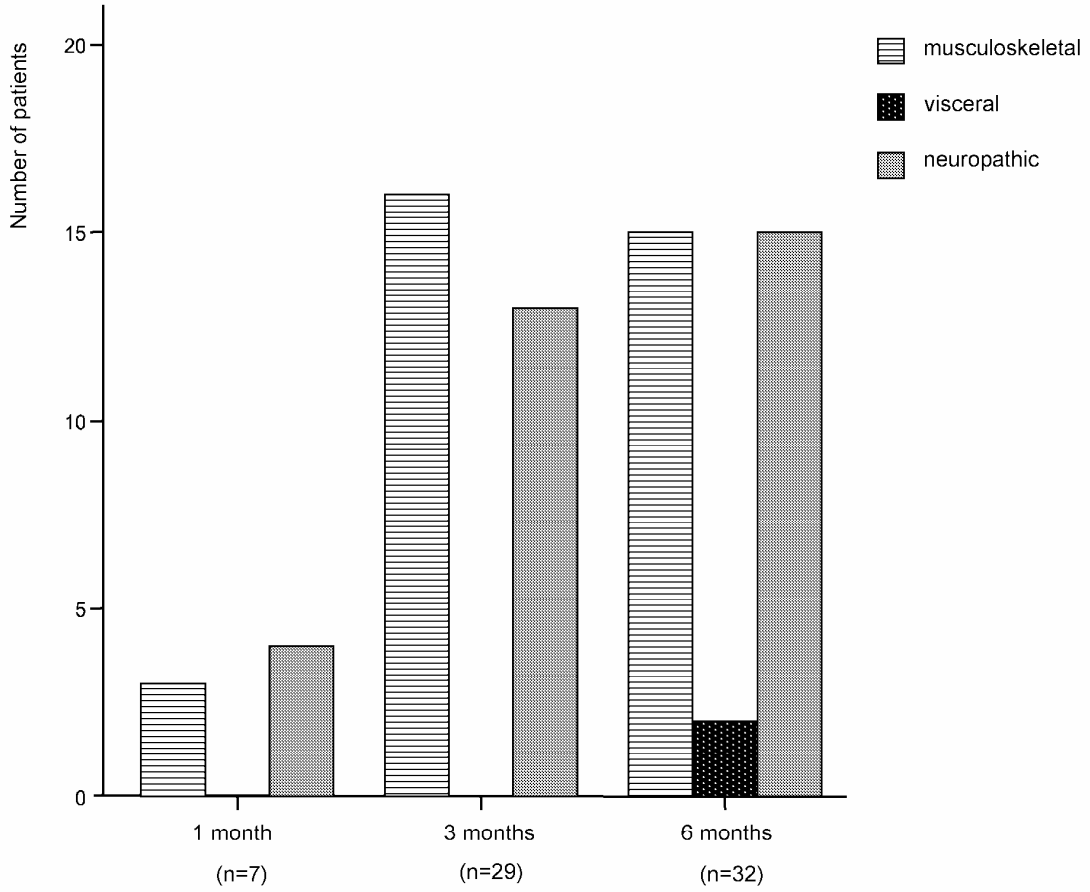

Figure 7: The histogram displays the number of subjects who experience musculoskeletal, visceral and neuropathic pain at 1, 3 and 6 months after spinal cord injury.

Comparison to other scales

The neuropathic pain group had a higher NPS score than the nociceptive pain group (p=0.07), however, this difference did not reach the significance level.

The score of the sensory part of the SES did not differ between the neuropathic and nociceptive group, although the descriptors burning, hot and tingling were significantly more frequently reported in the neuropathic group (Table 13). The score of the affective part of the SES was significantly higher in the neuropathic (23.8 ± 6.3) than in the nociceptive group (19.7 ± 5.5; p=0.05).

Table 13: Pain intensity and descriptors.

Groups	**Neuropathic pain (n=32)**	**Nociceptive pain (n=36)**
Present pain intensity	3.0 ± 2.4	1.9 ± 2.4
Mean pain intensity	4.4 ± 1.7	3.8 ± 1.9
Maximum pain intensity	6.5 ± 2.3	6.4 ± 2.0
Burning	1.84 ± 1.21 (n=18) *	1.41 ± 0.89 (n= 8)
Hot	0.29 ± 0.46 (n=13) *	1.32 ± 0.88 (n= 6)
Tingling	2.06 ± 1.24 (n=21) **	1.57 ± 0.98 (n=11)

Estimated pain intensity (mean ± standard deviation) on a NRS (0 to 10), as well as pain intensity and descriptors from the Pain Experiencing Scale (SES) for the two patient groups

***p < 0.05; **p < 0.01; ***p < 0.001**

Affective features of pain

More than 50% of the subjects rated their global health as excellent (17 subjects, 25%) or very good (29 subjects, 42.6%) and 15 as satisfying (22.1%). Negative health experience was reported by seven patients, bad by six (8.8%) and very bad by one (1.5%).

In the Pain-Report, scores for mood (6.9 ± 2.1), anxiety (2.7 ± 3.0), sleep quality (3.6 ± 3.0) and limitation in daily life (6.5 ± 2.6), rated on a NRS (0 to 10), did not differ between the two pain groups.

The correlation of data from single items of the Pain-Report and the MPI (e.g. “rate your overall mood” and “how tense or anxious have you been?”) revealed significant correlation coefficients for mood (r = .61, p=0.01) as well as for anxiety (r = .59, p=0.01).

From the whole sample, 25 patients (36.8%) showed mild to moderate severity of depression in the HAMD.

Discussion

The aim of the present study was to develop and test a practical SCI-specific pain screening tool. The results of our newly developed Pain-Report demonstrated that this tool is comprehensive, fast and simple to use, and is well accepted by the patients. In combination with the patient's neurological examination and the medical history, the Pain-Report covers sufficient information to reliably classify pain into nociceptive or neuropathic types. The Pain-Report has a high concordance with existing reports on pain assessments and further complements existing tools (Geissner, 1995; Kerns and Decker, 1985; Siddall et al., 2003; Siddall et al., 1999). In addition, the Pain-Report provides information about pain associated factors as affective factors, general well-being, and common sequelae of SCI.

Methodological considerations, strengths and limitations

The design and the items of the Pain-Report and of the recently published Pain Data Set (Widerstrom-Noga et al., 2008) have many similarities. The Pain-Report, which was developed before the publication of the Pain Data Set, contains additional features such as pain descriptors, allodynia and paraesthesia and more pain related factors. In addition, the present study is the first to publish clinical data, still lacking for the Pain Data Set.

The feasibility of the Pain-Report was confirmed by the speed of acquiring essential information about the patient condition and its acceptance by them, even shortly after injury. This might be partly due to its format as structured interview that was considered the best to quickly characterize pain. First, it has been shown that the psychometric properties are better covered in structured interviews than in self-rating questionnaires (Bennett, 2001). Second, a standardized interview facilitates follow-up assessments, even by telephone. This is important since the Pain-Report has been designed to be integrated into the EM-SCI that follows patients for at least one year. Third, the time frame of 10 minutes is excellent for clinical application in view of the patients' state. Finally, it can be applied for quadriplegic patients, who just have to answer, since they have difficulty filling out a self-report questionnaire.

As suggested by the NIDDR-group three classification systems are commonly used (i.e. IASP Taxonomy, Bryce/Ragnarsson SCI Pain Taxonomy and Cardenas SCI Pain Taxonomy) (Bryce et al., 2007). We preferred the classification proposed by the IASP

Task Force on Pain following SCI as it is supported by long-term studies of up to 5 years as well as in management approaches for chronic pain in clinical settings (Siddall et al., 2003; Siddall et al., 1999). The present data obtained in a structured interview gives support to this classification. In the field of pain assessment, the test-retest and inter-rater reliability are known to be low. For this reason, in the Pain-Report two independent raters classified the data of the same interview, rather than performing separate interviews. Indeed, our study showed a high level of agreement with an inter-rater reliability of 89% compared to the 79% previously reported agreements across pairs of raters (Putzke et al., 2003).

Despite of the criticisms to use verbal descriptors to classify pain types (Bouhassira et al., 2005), the pain classification provided by the Pain-Report strongly depends on verbal descriptors, as they are the most common means of classifying pain following SCI (Putzke et al., 2002c). In our opinion it makes sense to use such descriptors, since pain essentially is a subjective phenomenon. In the present study, patients classified by the Pain-Report as experiencing neuropathic pain, described their pain significantly more as burning, hot and tingling. Indeed, burning is a specific overall indicator of neuropathic pain in SCI patients (Putzke et al., 2002c). We were further able to confirm this finding by comparing the two groups using the same descriptors from the sensory part of the SES.

Comparison between neuropathic and nociceptive pain groups

Our grouping of the patients into a neuropathic and a nociceptive pain group, based on the IASP criteria, revealed that allodynia and paraesthesia are significant predictors for neuropathic pain. As expected, the NPS scores were higher in the neuropathic group, but statistically not significant, which might be explained by the relatively high variability between our (sub-acute) SCI patient groups. Indeed, the NPS was specifically developed for chronic patients experiencing neuropathic pain only. It therefore lacks features to distinguish neuropathic from nociceptive pain (i.e. allodynia and paraesthesia). At present the EMSCI network conducts a longitudinal study with the Pain-Report within the first year post injury. This will allow us to evaluate its sensitivity and compare the responsiveness of the Pain-Report and the NPS. At present, we suggest applying both tools in future studies.

Affective pain features

Pain interferes with rehabilitation, daily activities, quality of life, and may have significant influence on mood, leading to depression and even to suicide (Westgren and Levi, 1998). In contrast to these findings, more than 50% of the SCI patients in the present study rated their general well-being as good, despite the life-threatening circumstances.

Although the Pain-Report's single items assessing quality of life, mood and anxiety significantly correlated with the corresponding subscale of the MPI-D, we are aware that they are not sufficient to give a full account of these important psychological symptoms. The occurrence of these side effects should rather point to the necessity of additional investigations of the patient's mental state as we have been doing by applying the HAMD. The results scored with this depression inventory are in line with the literature reporting one third of SCI patients suffering from depression (Dryden et al., 2005) often without specification of its severity. In our sample, only mild to moderate depression was reported, which might be explained by the sub-acute time point of assessment.

Conclusions

With the Pain-Report, we present a descriptive and feasible clinical tool which can provide information about common pain features in accordance with current guidelines (IASP, 2001) (Bryce et al., 2007). In combination with neurological and medical information, the Pain-Report contains sufficient information for clinicians and researchers to differentiate between neuropathic and nociceptive pain, which is essential information for an appropriate pain treatment. At present, the Pain-Report is applied in a longitudinal study describing the time course of pain after SCI and evaluating its sensitivity to detect changes over time.

3.2. A prospective study of pain and pain related symptoms within the sub-acute phase after spinal cord injury (study 2)

Abstract

Study design: Prospective, longitudinal study.

Objective: Spinal cord injury (SCI) pain was classified according to the guidelines of the International Association for the Study of Pain. The incidence and prevalence, as well as course and changes of these pain types was evaluated within the sub-acute phase post injury.

Setting: European Multicenter Study for Human Spinal Cord Injury (EM-SCI).

Methods: At 1, 3 and 6 months post-injury 74 SCI patients were surveyed on experiencing pain using a standardized interview (Pain-Report).

Results: The prevalence of pain (any kind of type) was constant within the first 6 months (68%, 66%, and 65% respectively). By categorizing pain into musculoskeletal, visceral, and neuropathic pain it could be demonstrated that these pain types have further a different onset and follow individual courses. However, once a pain type is manifested it will likely persist, e.g. initial musculoskeletal pain persisted in 63% and initial neuropathic pain in 78%. Furthermore, allodynia was more related to below level pain (59%) whereas paresthesia was more common in at-level pain (69%). Except for anticonvulsants and spasmolytica, the nociceptive and neuropathic pain groups had the same intake of medication,

Conclusion: The prevalence of pain in SCI patients is high (65-68%) and remains stable during the sub-acute phase post injury. To optimize treatments and future interventions, the differentiation between pain types and the level of lesion (e.g. at- and below level neuropathic pain) is crucial as they relate to the onset and course, as well as specific sensory deficits such as allodynia and paresthesia.

Introduction

Pain is one of the most demoralising problems following spinal cord injury (SCI) and a challenging issue for researchers and clinicians. A prevalence rate of about 69% is known from literature (Bonica, 1991; Stormer et al., 1997; Siddall et al., 1999) and one third of these patients experience severe chronic, mostly neuropathic, pain (Siddall and Loeser, 2001).

Experiencing pain reduces quality of life (Rintala et al., 1998; Westgren and Levi, 1998; Widerstrom-Noga et al., 2001; Hammell, 2007) and can be more limiting than the consequences of the disability (Widerstrom-Noga et al., 2007). Furthermore, once a person develops pain, it is unlikely that the pain problem resolves on its own (Ehde et al., 2003) and at present, only a minority profits from treatments (Stormer et al., 1997; Ehde et al., 2003; Widerstrom-Noga and Turk, 2003). Indeed, the currently applied treatments might benefit from enhanced knowledge about the nature and cause of these pain syndromes and its underlying mechanisms

At present, only a few studies investigated the development of pain in a prospective way (e.g. Siddall et al., 2003; Jensen et al., 2005b). In particular research in the (sub-) acute phase of SCI has been neglected, as most studies focussed on chronic pain. It appears that changes in pain frequency and intensity over time are not associated with the duration and prevalence of pain (Demirel et al., 1998; Rintala et al., 1998; Jensen et al., 2005b; Siddall et al., 2003) and a variety of changes in pain during the first months or years after injury was reported, which requests further research on the time course of various pain types (Kennedy, 1997; Siddall et al., 2003; Jensen et al., 2005b).

Therefore, the aim of the present study was twofold: First, to observe the prevalence and development of pain after SCI and, second, to focus on the changes in pain over time in the sub-acute stage, i.e. within the first six months after SCI. Pain and pain related factors were prospectively assessed at fixed time points after SCI by means of a structured interview. We hypothesize, based on clinical experience and a small number of studies (Siddall et al., 2003; Jensen et al., 2005b) that nociceptive pain has a high occurrence initially and decreases during the sub-acute phase, while the development of neuropathic pain progresses with time.

Methods

Patients participated in the European Multicenter Study for Human Spinal Cord Injury (EM-SCI; www.emsci.org) (Curt et al., 2004). Within the EM-SCI, patients are assessed at five standardized stages. For the present study we focused on three stages, 1 month (16-40 days), 3 months (70-98 days) and 6 months (150-186 days) post injury. Patients suffered from a primary SCI due to ischemia or trauma. Exclusion criteria were reduced capabilities of cooperation or giving consent (e.g. dementia, psychological disorders and language barriers), peripheral nerve lesions above the level of injury or severe brain injuries.

The various aspects of pain were surveyed using the Pain-Report. This screening tool is a standardized interview and took approximately 10 minutes.

The Pain-Report contains 16 items that assess clinically relevant information concerning pain (e.g. three descriptors for each pain type, onset, frequency, pain intensity assessed on 0-10 numeric rating scale (NRS), and pain reducing and triggering factors). In addition, 7 items assess relevant pain cofactors like mood, anxiety, quality of sleep, daily limitations and a ranking of the impact of common SCI sequelae.

Pain was classified into four categories according to location, description and apparent origin as described by (Siddall et al., 1997). This classification system was later integrated as the three tier taxonomy by the IASP (2001) and can be considered at present the international standard (Dworkin et al., 2005); Bryce et al., 2007; Alexander et al., 2009). In our study, pain was classified on tier 1 and 2.

Pain categorization was performed by a trained psychologist who combined the information gathered from the Pain-Report with the medical history and the neurological status according to the American Spinal Injury Association (ASIA, 2002) In the EM-SCI, assessors receive twice per year an ASIA training, to improve the skills for the assessment and classification of the neurological impairment; although the classification is also performed by a computer algorithm (see also Spiess et al., 2009). All data were compiled in a central database. The study was approved by the local ethics committee and conformed to the Declaration of Helsinki.

Data analysis

The patients were grouped into neuropathic (e.g. at- and below level of lesion) and nociceptive pain (e.g. musculoskeletal and visceral pain). In general, data are expressed as mean and standard deviation (SD). For group comparisons, chi-square methods and the Friedman test was used. The level of significance was set at 0.05. The data were analyzed using SPSS Version 14.0.2 for Windows.

Results

The sample consisted of 74 SCI patients whose demographic information is listed in Table 14. Within the 6 months time period, 34% of the SCI patients remained painless, 29% developed musculoskeletal and 37% neuropathic pain; thereof 16% with below level pain and 21% with at-level pain. Thirty-four (46%) patients experienced two pains; 16 were categorized as musculoskeletal and 18 as neuropathic, while 6 (8%) patients reported 3 different pains. The present study evaluated only the most prominent pain.

The number of patients without pain remained stable over time, e.g. 32% at 1 month, 34% at 3 months and 35% at 6 months post injury. The prevalence of musculoskeletal pain decreased over time from 32% to 23%. Into more detail, musculoskeletal pain due to bone, joint, muscle trauma or inflammation decreased from 20% at 1 month to 6% at 6 months, while overuse syndromes increased from 9% to 15% in the 6 months period.

Neuropathic pain (including at- and below level pain) was present at 1 month in 32% of the patients and increased to 42% at 6 months. The differentiation according to the level of lesion revealed a stable prevalence of at-level pain, while below level pain increased from 10 to 15 patients within 6 months (illustrated in Figure 8).

However, as such a general analysis might not reflect the changes of the most prominent pain within each patient; we presented a pain matrix (see Table 15). Sixty-three percent of the patients without pain at 1 month post-injury were unlikely to develop pain at a later stage Noticeable are the high number of patients suffering from the same pain type during all three stages (bold). Patients experiencing neuropathic (at- and below level) pain in the initial phase, reported also neuropathic pain at 6 months after injury (78%). Less than 20% of those who were not experiencing pain within the first month after injury developed neuropathic pain at a later stage.

Table 14: Patient's demographic characteristics.

Descriptives	**Numbers**
Gender	
Male	62 (83.8%)
Female	12 (16.2%)
Etiology	
Traumatic	72 (97.3%)
Ischemic	2 (2.7%)
Injury	
Paraplegic	37 (50%)
Tetraplegic	37 (50%)
Neurological Impairment (initial stage)	
ASIA A	29 (39.2%)
ASIA B	8 (10.8%)
ASIA C	13 (17.6%)
ASIA D	24 (32.4%)
Age [years] at injury (mean ± SD)	43 ± 18.61 (13-83)

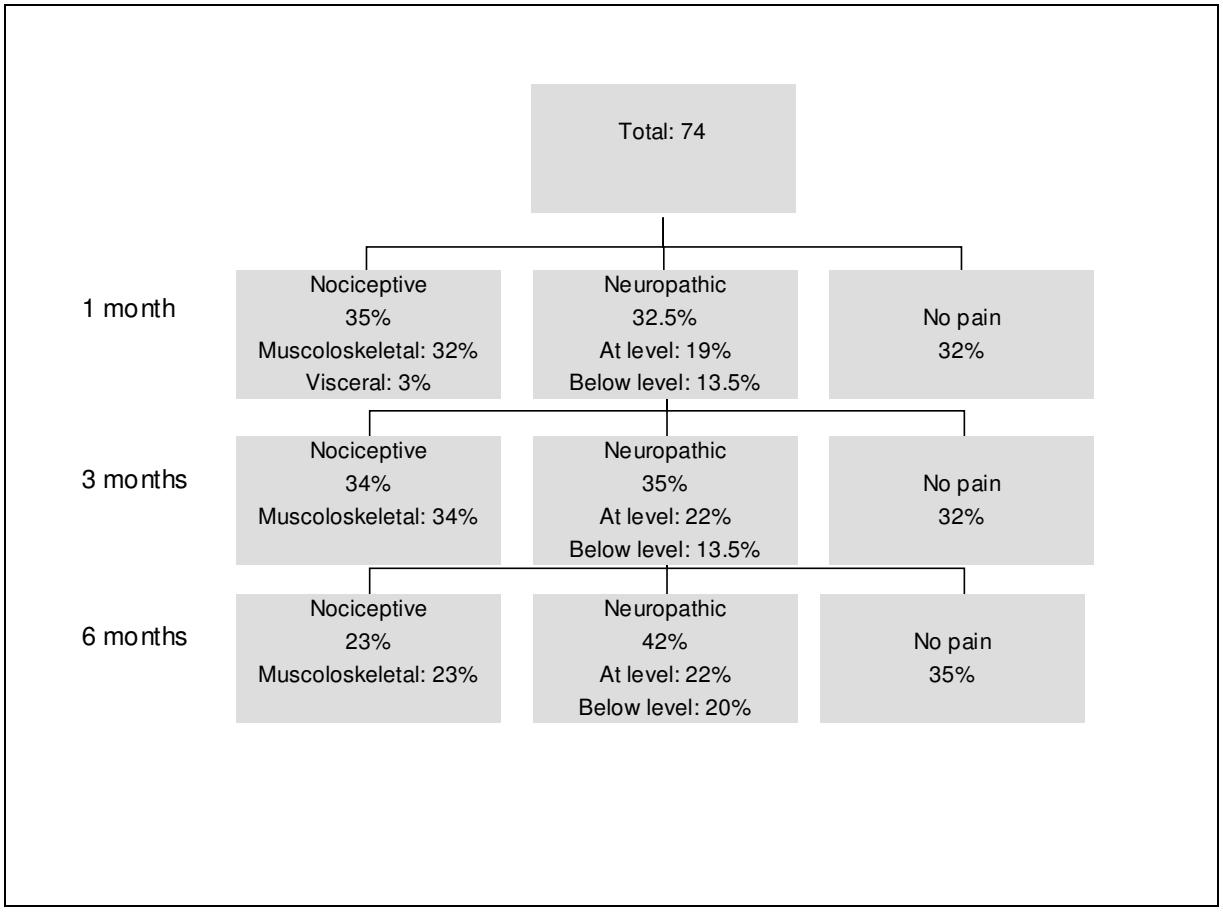

Figure 8: Prevalence of pain types within the first 6 months.

Table 15: Shift in the most prominent pain (pain matrix).

No pain at 1 month	**N**	**Musculoskeletal pain at 1 month**	**N**	**Neuropathic pain at 1 month**	**N**
0-0-0	**11**	1-0-0	1	3-0-1	1
0-1-0	4	1-0-1	2	3-1-0	1
0-0-1	1	1-1-0	4	3-1-3	2
0-1-1	3	**1-1-1**	**8**	3-0-3	1
0-0-3	2	1-0-3	3	3-3-0	1
0-3-3	3	1-1-3	2	3-3-1	2
		1-3-1	1	**3-3-3**	**15**
		1-3-0	1		
		1-3-3	3		
Total	***24***		***25***		***23***

Changes in most prominent pain at 1 month for the three groups: no pain (0), musculoskeletal pain (1) and neuropathic pain (3). For example, the code 0-0-0 describes that this patient did not experience SCI related pain at 1, 3 and 6 months. The code 3-1-3 described that the most prominent pain in these subjects was categorized as neuropathic pain at 1 and 6 months, but musculoskeletal pain at 3 months after SCI. Abbreviations: N, number. Note: the total is 72 since this analysis is calculated without those experiencing visceral pain.

Pain intensity and localisation

Pain intensity was calculated at each time point for patients grouped in nociceptive and neuropathic pain (see Figure 9). The rated pain intensity as well as the localization of pain was similar at the three time points. In both groups, the most reported regions in all three time stages were shoulders, arms and hands (see Table 16).

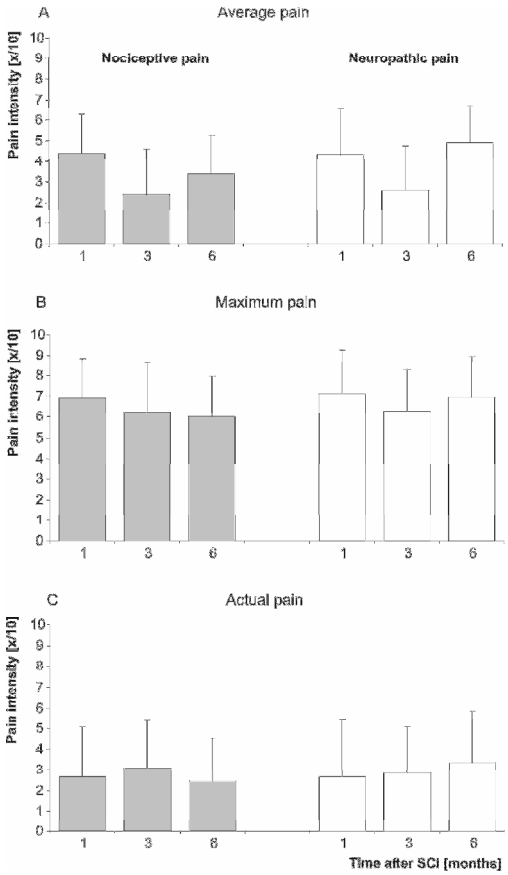

Figure 9: Average, maximal and actual pain intensity separately for the nociceptive pain group and the neuropathic pain group.

	1 month	3 months	6 months
head	0%	0%	0%
neck	5.4%	6.7%	9.5%
shoulders	31.4%	35.1%	25.7%
arms	16.2%	17.6%	14.9%
hands	20.3%	20.3%	20.3%
back	8.1%	8.1%	9.5%
cross	18.9%	13.5%	9.5%
fundament	8.1%	4.0%	4.0%
shanks	10.8%	9.5%	16.2%
feet	4.0%	8.1%	8.1%

Table 16: Body areas of experienced pain.

Allodynia and paraesthesia

Allodynia and paresthesia were reported more frequently in patients with neuropathic pain. One third of the neuropathic pain group did not experience allodynia or paraestesia, whereas about 10% of the patients experiencing musculoskeletal Pain-Reported coexistent allodynia and paraesthesia. Clearly, the majority of patients with musculoskeletal pain (65%) reported neither allodynia nor paraesthesia.

The appearance of allodynia and paraesthesia increased in the neuropathic pain group from 25% at 1 month to 32% at 6 months, but decreased in patients with musculoskeletal pain from 12.5% to 5%. Paraesthesia was more common than allodynia at each time stage, in both pain groups (Table 17).

Table 17: The appearance of allodynia and paresthesia according to time points and illustrated separately for the nociceptive and the neuropathic pain group.

	1 month	3 months	6 months
Neuropathic	*n=24*	*n=26*	*n=31*
Allodynia + Paresthesia	21% (n= 5)	15% (n= 4)	32% (n=10)
Allodynia	8% (n= 2)	15% (n= 4)	9% (n= 3)
Paresthesia	33% (n=8)	35% (n= 9)	35% (n=11)
None	37.5%(n= 9)	35% (n= 9)	22% (n= 7)
Nociceptive	*n=26*	*n=23*	*n=17*
Allodynia + Paresthesia	15% (n= 4)	8% (n= 2)	5% (n= 1)
Allodynia	8% (n= 2)	4% (n= 1)	17% (n= 3)
Paresthesia	4% (n= 1)	26% (n= 6)	24% (n= 4)
None	73% (n=19)	60% (n=14)	53% (n= 9)

Abbreviations: n total number of pain type in current time point; (n) number of patients who sustain allodynia or paresthesia in current time point.

Intake of medication

By all means, pain intensity, allodynia and paraesthesia might have been influenced by the intake of medication. The course of medication consume was different within 6 months. NSAID's showed a decrease from initial 63% to 38% at 6 months after SCI (p=0.01), as well as antidepressants (28% to 17%), opiates (31% to 15%) (p=0.19) and hypnotics (21% to 15%). A strong increase in the intake of anticonvulsants (from 8% to 26%, p=0.03) and anti-spasticity medication (from 4% to 24%, p=0.01) was observed, especially in the neuropathic pain group.

Discussion

To our knowledge, this was the first longitudinal study investigating the prevalence of pain at fixed time points after SCI in a cohort of European (across countries) SCI patients. The prevalence of the classified pain types is in line with the results from previous studies (Bonica, 1991; Stormer et al., 1997; Siddall et al., 2003; Siddall et al., 1999), which validates these current findings. While most studies reported the onset of pain within the first 6 to 12 months after injury (Stormer et al., 1997; Siddall et al., 1999; Siddall et al., 2003), here, 54% of those reporting pain at 1 month post-injury were also complaining at 6 months. In addition, a large percentage of those without pain at 1 month after SCI, did not complain about pain at 6 months post-injury. Indeed, this is important with respect to possible treatment interventions, as several studies confirmed that once a person develops pain, it is likely to persist (Kennedy, 1997); (Ehde et al., 2003). Yet, the relative high stability of these pain types in the present study might be surprising, as previous studies reported a high variability in the onset of pain, while severity and intensity could change unpredictably (Stormer et al., 1997; Kennedy, 1997; Vogel, 2002).

This study confirmed our hypotheses that nociceptive pain has a high occurrence initially and decreases during the sub-acute phase, while the development of neuropathic pain progresses with time. The finding that a high percentage of SCI patients with neuropathic pain at 1 month post-injury still have neuropathic pain at 6 months might urge the rehabilitation specialist to perform a pain interview early during rehabilitation. As neuropathic pain after SCI continues or even worsens over time (Stormer et al., 1997) and patients who experience neuropathic pain 3 to 6 months after SCI still experience pain at 3-5 years post injury (Siddall et al., 2003), an aggressive pain treatment is indicated in order to prevent development of pain in the first 6 months post injury (Jensen et al., 2005b) or, according to the present results, even earlier.

Incidence of pain types

The overall percentage of SCI patients with *neuropathic pain* increased within the first 6 months after SCI, which was mainly based on an increase in below level pain, while the occurrence of at-level pain remained relatively constant. Indeed, previous studies confirmed that at-level pain has an earlier onset (mean 1.2 years post injury) than below level pain (mean 1.8 years) (Jensen et al., 2005b).

The different onset and course of the pain levels in neuropathic pain demonstrates the importance of its distinction (Yezierski, 2005) and points toward different mechanisms. Below level neuropathic pain is considered to be a central pain condition caused by spinal cord damage, while at-level pain might have peripheral and central components that are difficult to separate (Siddall et al., 1997; Finnerup et al., 2003).

Musculoskeletal pain is common in acute as well as in chronic stages after SCI (Siddall et al., 2003). In our study, pain due to musculoskeletal trauma decreased during 6 months from 20% to 6%,. In contrast pain due to overuse syndromes increased from initially 9% to 15% and is considered an established observations from clinical daily life (Ballinger et al., 2000; Goldstein, 2000; Vogel, 2002; Jensen et al., 2005b).

Visceral pain is usually described as a dull or cramping pain, mostly located in the abdominal region. In the present study, the prevalence of 2.7% was even less than reported previously (i.e. between 5 to 38%, see (Anke et al., 1995; Stormer et al., 1997; Ng et al., 2005). The small prevalence in the present study could be explained by the late onset that has been described varying from 4.2 years (Jensen et al., 2005b) to 5 – 10 years post injury (Siddall et al., 2003; Kogos et al., 2005; Finnerup et al., 2008). The late onset of visceral pain could be due to defecation frequency and constipation (Finnerup et al., 2008).

Allodynia and paresthesia

Allodynia and paresthesia were only assessed in patients who reported pain, as allodynia appears to be more common in painful than in non-painful areas (Eide et al., 1996). The appearance of allodynia and / or paresthesia remained stable within 6 months post injury in this sample (Ehde et al., 2003; Siddall et al., 2003) and was more frequent in patients with neuropathic pain, as also reported by (Finnerup et al., 2001). In the neuropathic pain group, the combined appearance of allodynia and paraesthesia as well as the isolated appearance of paraesthesia increased over time, while isolated allodynia slightly decreased. By dividing neuropathic pain according to the level of injury different characteristics could be observed. Whereas allodynia was more related to below level pain compared to at-level pain (59% and 21% respectively) paresthesia was more common in at-level compared to below level pain (69% and 51% respectively). Remarkably, allodynia and paraesthesia were also reported in patients with

musculoskeletal pain. For both neuropathic and musculoskeletal pain groups the distinction between allodynia and paraesthesia could be relevant, as allodynia is often related to severe complaints, while paresthesia appears not to be unpleasant (Finnerup and Jensen, 2004).

Pharmaceutics

While anticonvulsants and anti-spasticity medication were more consumed in the neuropathic group, no additional differences in medication intake between the two main pain groups could be demonstrated. The intake of non-steroidal anti-inflammatory drugs (NSAIDs), opiates, hypnotics and anti-depressive medication, which are often prescribed in the acute phase (Warms et al., 2002; Widerstrom-Noga and Turk, 2003) were found to decrease within the first 6 months. On the contrary, the intake of anticonvulsants and anti-spasticity medication increased, which might be related to the increased prevalence of below level neuropathic pain at six months (Hempenstall and Rice, 2002).

Methodological considerations

Due to the selection criteria of the EM-SCI, some characteristics of the present subject sample could differ from the general SCI population (see Wyndaele and Wyndaele, 2006). The SCI patients in the present study were on average older and the origin of the SCI in most subjects in this study was of a traumatic nature (normally about 50%). Still, we assume that the present findings might be generalized to especially the SCI population, especially with a traumatic origin.

Furthermore, as stated previously, we focused on the presence and intensity of the strongest pain, whereas the number of pains experienced was not considered. Indeed, this might explain some of the results in which the most prominent pain changed from neuropathic to musculoskeletal or vice versa.

Conclusion

The present study confirmed that the prevalence of neuropathic pain increases in time to become the most frequent occurring pain type after SCI (Stormer et al., 1997; Siddall and Loeser, 2001; Siddall et al., 1999). Both the presence of neuropathic pain and the absence of pain at 1 month after injury might allow an early prediction concerning the presence of (neuropathic) pain at 6 months. Unfortunately, most patients with

neuropathic pain in the sub-acute phase develop chronic pain and will suffer from their condition, despite using pharmaceutics. These results point to early detection, i.e. within the first months, and intervention of pain after SCI to prevent a chronification of the pain syndrome.

3.3. Pain and depression hardly affect daily life activities within the first year after spinal cord injury (study 3)

Abstract

The aims of the study were to investigate whether pain and / or depression have a negative impact on the performance of daily life activities (ADL) within the first year after spinal cord injury (SCI) and whether the objective level of ADL performance corresponds to the perceived level of interference. Eight European centers assessed subject characteristics (e.g. age), the neurological impairment level (ASIA) and ADL with the Spinal Cord Independence Measure (SCIM) of 173 persons at 1, 3, 6 and 12 months after SCI. Additionally, the intensity and frequency of pain, the Beck Depression Inventory (BDI) and the perceived interference with ADL were examined. Regression models were used to evaluate the influence of pain and depression on the SCIM scores, beyond the proportion explained by the neurological impairment and age. The ASIA motor score and age explained 40% (1 month) to 81% (6 months) of the SCIM scores. While the pain measures did not contribute to the model, the BDI score contributed up to a level of 6% at 12 months. The reported interference with ADL correlated poor to moderate with the SCIM score ($r_s \leq -0.48$). We conclude that pain did not negatively affect the performance of ADL within the first year after SCI, while the severity of depression did at 12 months post-injury. In addition, perceived interference should not be used as a replacement for actual disability, which is important for ongoing discussions concerning the best outcome measure for clinical trials: activity or participation based.

Introduction

The neurological and functional recovery after a spinal cord injury (SCI) can be assessed by various measures at the level of body functions and – structures, such as the International Standards (ASIA, 2002) to evaluate sensory and motor recovery. At the activities level, capacity tests such as the 10 meter walk test (van Hedel et al., 2005) can be performed, as well as performance tests that assess activities of daily life and independence, such as the Spinal Cord Independence Measure (SCIM; Catz et al., 1997; Catz et al., 2001; Catz et al., 2007).

However, besides the evaluation of neurological and functional recovery, patients with SCI complain about pain, a symptom that is difficult to assess due to its complexity. SCI-specific pain can roughly be categorized into nociceptive pain, comprising of musculoskeletal and visceral pain, and neuropathic pain that can occur above, at, or below the level of lesion (see the International Association for the Study of Pain; see Siddall and Loeser, 2001) or for review (Finnerup and Jensen, 2004). In general, SCI-related nociceptive pain can occur as a direct result of the incident, or might develop over time due to overuse, for example musculoskeletal shoulder pain due to frequent manual wheelchair use in persons with a tetraplegia (e.g. Siddall et al., 2003). The presence of neuropathic pain is likely related to a (partial) lesion of the spinothalamic tract (Boivie, 1989; Vestergaard et al., 1995) and neuropathic pain below the level of lesion is often accompanied by hyper-sensitivity around the level of lesion (Finnerup et al., 2003; Finnerup et al., 2007). In general, neuropathic pain takes time to develop, although in some cases, neuropathic pain could occur early during rehabilitation (e.g. due to root compression at the site of the lesion) (Siddall et al., 2003). Although the exact mechanism leading to neuropathic pain remains largely unknown, it is generally agreed that pain can interfere with rehabilitation and with the performance of daily life activities in SCI patients, thus severely impacting quality of life (Budh and Osteraker, 2007; Middleton et al., 2007; Putzke et al., 2002b; Westgren and Levi, 1998; Hammell, 2007).

Furthermore, pain can have a significant influence on mood, leading to depression and even to suicide (Rintala et al., 1998; Segatore, 1994; Westgren and Levi, 1998), for review see Craig et al. (2009). Indeed, it has been reported that about 30% of SCI patients suffer from a (mild) depression disorder during rehabilitation (e.g. Kennedy and Rogers, 2000b); for review see Craig et al. (2009). The severity of the depression not only influences the performance of daily life activities in SCI persons living in the

community (MacDonald et al., 1987), but also appears to influence the functional outcome of the rehabilitation process (e.g. Malec and Neimeyer, 1983).

This latter point, however, is unclear, as most studies have investigated the influence of pain and depression in community-based samples and, in general, the subjective interference according to the person and not the objective level of performance has been assessed. Therefore, the aims of this study were twofold: (i) to assess the influence of pain and depression on the performance of activities of daily life within the first year after a SCI, beyond the proportion that might be explained by the neurological deficit and individual characteristics and (ii) to determine whether the objective level of performance of daily life activities corresponds to the perceived level of interference in persons with SCI.

Methods

2.1 Persons with spinal cord injury

Eight centers agreed to participate in the pain assessment project within our European Multicenter Study for Human Spinal Cord Injury (EM-SCI; see Curt et al., 2004) network. Within the EM-SCI, data are prospectively assessed after SCI. As the rate of recovery diminishes as time elapses (e.g. Waters et al., 1993; Waters et al., 1992), the persons with SCI were assessed at the following five stages: stage 1 within the first 15 days post-injury, stage 2 at one month (16-40 days), stage 3 at three months (70-98 days), stage 4 at six months (150-186 days) and stage 5 at twelve months (300-400 days). Patients with reduced capabilities for cooperation or for giving consent (e.g. dementia, psychological disorders and language barriers), peripheral nerve lesions above the level of injury or severe brain injuries were not included in the database. This study was approved by the local ethics committee and was performed in accordance with the declaration of Helsinki.

2.2 Assessment of daily life activities and independence

The SCIM is at present the preferred tool to assess activities of daily life and independence in persons with SCI (Alexander et al., 2009). It contains three subcategories: (i) self-care (e.g. bathing, grooming and dressing the upper and lower body), (ii) respiration and sphincter management (e.g. bladder and bowel management)

and (iii) mobility (e.g. transfer from bed to wheelchair, as well as mobility indoors and outdoors). The SCIM has been revised twice since its first introduction in 1997 (Catz et al., 1997), namely in 2001 (SCIM II, Catz et al., 2001) and 2007 (SCIM III, Catz et al., 2007). In these revisions, single items were changed or deleted, but the sum scores of the categories and the total score remained the same. As we switched within the EM-SCI at a certain point from SCIM II to SCIM III, some persons in this study were initially, and therefore also repeatedly, assessed with the SCIM II, while others were scored with the SCIM III.

2.3 Assessment of neurological impairment

The neurological assessment is performed in accordance with the International Standards (ASIA, 2002). The International Standards provide information about the completeness of the lesion and the sensory, motor and neurological level of the lesion. It enables the categorization of persons with SCI: ASIA A, sensory-motor complete; ASIA B, motor complete, but sensory incomplete; ASIA C, sensory-motor incomplete, with the average strength of the muscles below the level of lesion less than 3 (i.e. movement over the full range of motion against gravity) and ASIA D, sensory-motor incomplete, but with the average muscle strength equal to or above 3. The key point of each dermatome is scored for light tough and pin prick (0, absent; 1, impaired and 2, normal). Muscle strength is assessed for five upper and five lower extremity muscle groups and scored on an ordinal scale between 0 (no contraction) and 5 (movement over the full range of motion, against gravity and strong resistance). Sum scores can be calculated for the sensory scores (maximally 112 points) and motor score (maximally 100 points).

To ensure a high examination quality of the neurological assessment, the assessors are trained within the EM-SCI to standardize the examination techniques. Two annual 2-day trainings (one in German and one in English) are performed and progress in classification skills is documented by pre-, and post-testing. Moreover, to ensure objective and reliable processing of the gathered data, the AIS classification is performed by a computer algorithm (see Spiess et al., 2009). This method proved to be 100% correct when compared to the original training cases from the Philadelphia ASIA workshops, if no optional assessments such as hip flexors are required.

2.4 Assessment of pain

Pain was assessed by means of a structured interview, the Pain-Report, that is in agreement with the recommendations of the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT, see Dworkin et al., 2005; Turk et al., 2006). The Pain-Report allows the combined assessment of pain severity as well as physical and emotional functioning to capture the multi-dimensionality of pain. The Pain-Report contains 23 items, of which 16 define aspects of pain and 7 coherent pain factors. The assessment was performed in each center by local staff, after which the data was entered into the local database and was then sent to the central database at Balgrist University Hospital. Here, the pain categorization was performed by a trained psychologist who combined the information derived from the pain interview with information about the neurological status of the patient and the history of the patient. Although patients might experience various pains, the present paper evaluated only the influence of the most prominent pain on functional outcome.

For the present study, we were interested in the following pain variables: (i) the intensity of pain, quantified using an 11-point Numerical Rating Scale (NRS), at the time of the examination, as well as the average and maximum pain intensity during the last week, (ii) the frequency of pain (never, "0"; monthly, "1"; weekly, "2"; daily, "3" and permanently, "4") and, (iii) the presence of pain (no, "0"; yes, "1"). In addition, we evaluated the score of their perceived general restrictions on their everyday life on a scale from 0 (none) to 10 (major restrictions). This question was formulated as such that is was not restricted to interference of daily life activities due to pain, but in general to the SCI.

2.5 Assessment of depression

The Beck Depression Inventory (BDI) was first published in 1961 (Beck et al., 1961). Twenty-one symptoms and attitudes were derived from the clinical observations and the intensity of each item was rated from 0 to 3. The items were chosen to assess the intensity of depression and were not selected to reflect a particular theory of depression. The 21 symptoms and attitudes are: mood, pessimism, sense of failure, lack of satisfaction, guilt feelings, sense of punishment, self-dislike, self-accusation, suicidal wishes, crying, irritability, social withdrawal, indecisiveness, distortion of body image, work inhibition, sleep disturbance, fatigability, loss of appetite, weight loss, somatic preoccupation and loss of libido. A total score can be calculated by summing up the

individual scores of the 21 items. Cut-off scores were made to determine the severity of the depression: none or minimal depression is < 10; mild to moderate depression is 10-18; moderate to severe depression is 19-29; and severe depression is 30-63. The BDI has been proven useful in the SCI population, as shown in several studies (Craig et al., 2009; Craig et al., 1994; Hancock et al., 1993; Kennedy and Rogers, 2000b; Malec and Neimeyer, 1983; Richards, 1986).

2.6 Statistics

Various statistical analyses that quantify relationships were performed. Simple linear relationships were quantified using Pearson's (r) or Spearman's (r_s) correlation coefficient, when appropriate. In addition, multiple linear regression analysis was performed, in which the dependent variable was the sum score of the SCIM. As in previous studies, we used a hierarchical approach (Rintala et al., 1998). First, we entered the ASIA motor score (i.e. the sum of the strength of the ASIA key muscles) as an independent variable into the model, followed by the second variable age. In the third step, we entered the actual pain intensity and the pain frequency in the model. In additional models, this final step was repeated to evaluate the combination of average pain intensity and pain frequency, maximal pain intensity and frequency, the presence of pain and, finally, the BDI total score. The change in the explained variance during the final step of this regression approach could be defined as the proportion of functional outcome that can be attributed to pain intensity and frequency or the severity of depression, respectively. These analyses were repeated for each time point separately.

Results

3.1 Description of the persons with SCI

The characteristics of the persons with SCI are shown in Table 18. The 173 persons were admitted for rehabilitation between December 2006 and January 2009 to the following centers: Barcelona, Spain, 7 persons; Halle, Germany, 33; Heidelberg, Germany, 9; Hessisch-Lichtenau, Germany, 1; Langensteinbach, Germany, 11; Murnau, Germany, 45; Ulm, Germany, 24 and Zurich, Switzerland, 41 persons. Several

persons were assessed repeatedly (2 to 4 times) at the several assessment points, explaining the higher number of measurements compared to the number of persons (Table 18). The average length of stay was 4.2 ± 3.0 months, although data of 79 persons was missing due to still being in-patient or incomplete records.

Table 18: Characteristics of the subjects included in this study.

Variable	Time after spinal cord injury			
	1 Month N = 151	**3 Months N = 132**	**6 Months N = 87**	**12 Months N = 40**
Gender [f/m]	26 / 125	25 / 107	13 / 74	5 / 35
Age [years]	47 ± 19	46 ± 19	46 ± 20	43 ± 18
Height [cm]	176 ± 8	175 ± 8	176 ± 8	176 ± 8
Cause [ischemia/trauma]	8 / 143	8 / 124	4 / 83	3 / 37
Lesion level [tetra/para]	72 / 74	63 / 67	41 / 45	26 / 13
AIS [A/B/C/D]	52 / 17 / 20 / 50	46 / 12 / 15 / 49	28 / 8 / 30 / 76	8 / 3 / 3 / 16
ASIA motor score [x/100]	55 ± 26	61 ± 26	62 ± 28	70 ± 28
SCIM sum score [x/100]	29 ± 25	52 ± 28	64 ± 29	75 ± 26
Pain now [x/10]	1.4 ± 2.2	1.6 ± 2.1	2.1 ± 2.6	2.6 ± 2.6
Average pain [x/10]	2.7 ± 2.8	2.4 ± 2.5	2.7 ± 2.7	3.2 ± 2.8
Maximum pain [x/10]	4.2 ± 3.7	4.1 ± 3.7	4.3 ± 3.7	4.5 ± 3.6
Pain frequency [n / m / w / d / p]	51 / 0 / 3 / 47 / 36	48 / 1 / 6 / 46 / 24	29 / 0 / 4 / 28 / 21	12 / 0 / 3 / 10 / 14
Pain category [noci / neuro]	53 / 39	38 / 42	21 / 37	12 / 14
BDI score	8.5 ± 6.7	7.0 ± 5.2	6.7 ± 5.9	9.1 ± 6.1

Presented are absolute numbers or means ± standard deviations. Please note, due to missing values, the numbers might not sum up to the total numbers. Abbreviations: tetra, tetraplegic; para, paraplegic; AIS, ASIA Impairment Scale; SCIM, Spinal Cord Independence Measure; n, never; m, monthly; w, weekly; d, daily; p, permanently; noci, nociceptive pain; neuro, neuropathic pain; BDI, Beck Depression Inventory.

3.2 Neurological and functional measures

Although the size and consistency of the groups of persons with SCI were different between the several time points, the neurological scoring, represented by the ASIA motor score and the performance of daily life activities, represented by the SCIM total score, appear to be higher at later time points (Table 18). To get an insight into the range of the SCIM total score, see also Figure 10.

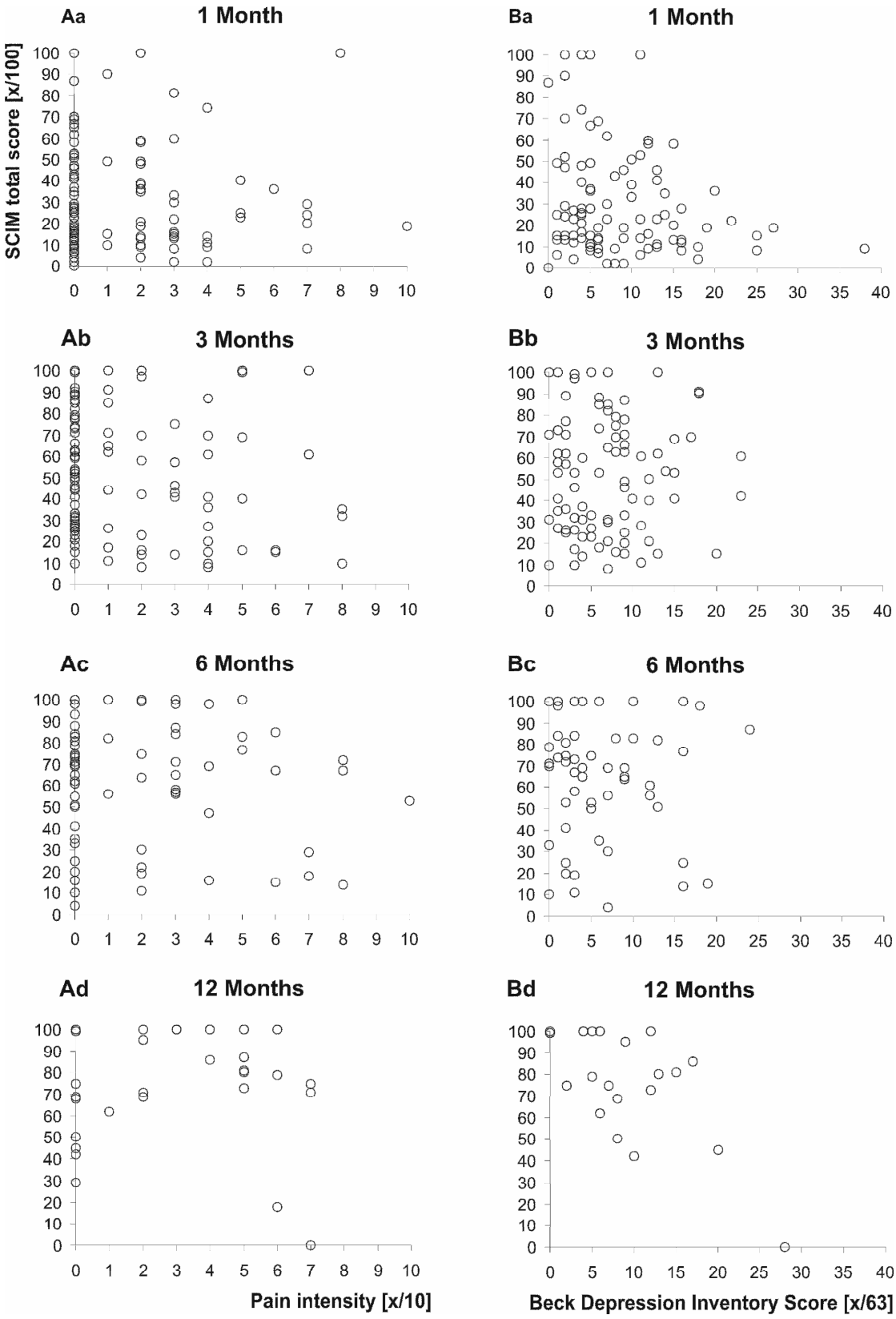

Figure 10: Relationships between activities of daily life, pain and depression scores Scatter-plots showing the relationship between the total score of the Spinal Cord Independence Measure (SCIM) versus (A), pain intensity and (B), the Beck Depression Inventory score at (a), 1 month, (b), 3, (c), 6 and (d), 12 months after spinal cord injury.

3.3 Pain scores

About one-third of the persons with SCI did not experience pain (see also Table 18) and the percentage of patients who experienced pain was comparable between the assessment points (1 month, 63%; 3 months, 62%; 6 months, 64%; 12 months, 69%). Overall, the average pain intensity (persons without pain were included in the calculation) was higher at later time points. While the actual pain level was almost twice as high at 12 months when compared to the 1 month assessment, differences were smaller for the average and maximum pain levels. The average maximal pain levels were just above 4 at all time points, an intensity which can be considered as considerable. The ratio of persons with iSCI categorized with nociceptive versus neuropathic pain varied between the time points (1 month, 1.36 to 1.00; 3 months, 0.90 to 1.00; 6 months, 0.57 to 1.00; and 12 months, 0.86 to 1.00, see also Table 18).

3.4 Depression scores

The mean DBI scores are presented in Table 18. At 1 month after SCI, most persons with SCI (72 out of 117, i.e. 61.5%) did not have a depression (BDI score < 10; see also Figure 1B). A mild depression (9 < BDI score < 19) was observed in 37 persons (31.6%), while 7 (6.0%) experienced a moderate depression (18 < BDI score < 30) and 1 (0.9%) a severe depression (BDI score > 29). At 3 months after SCI, 83 out of the 109 persons (76.1%) did not have a depression, 22 (20.2%) experienced a mild depression and 4 (3.7%) a moderate one. At 6 months after SCI, the results were similar. Fifty-two persons out of 70 (74.3%) did not have a depression, 14 (20.0%) experienced a mild and 4 persons (5.7%) a moderate depression. Finally, at 12 months after SCI, 19 out of 29 persons (65.5%) did not have a depression, 8 persons (27.6%) suffered from a mild depression and 2 (6.9%) from a moderate.

3.5 Relating performance of activities of daily life with pain and depression

No statistically significant correlation between the SCIM total score and pain intensity were observed (for example for the actual pain intensity, the Spearman correlations amounted to: r_s = -0.02, P = .81, N = 119 at 1 month; r_s = -0.12, P = .19, N = 113 at 3 month; r_s = -0.05, P = .66, N = 73 at 6 months; and r_s = 0.17, P = .36, N = 31 at 12 months). The correlations with the average and maximal pain were of comparable magnitude. The correlations with pain frequency were similarly small, but in general positive.

The correlations of SCIM with the BDI score were comparable to those with pain, except at 12 months after SCI, where there was a statistically significant correlation (r_s = -0.16, P = .12, N = 95 at 1 month; r_s = -0.06, P = .59, N = 93 at 3 month; r_s = -0.10, P = .47, N = 58 at 6 months; and r_s = -0.50, P = .02, N = 21 at 12 months).
However, as possible relationships between the SCIM total score and the pain intensity or depression scores might have been masked by differences in neurological status and age, multiple linear regression analyses were performed to determine the influence of pain or depression beyond the influence of the neurological impairment or age.

3.6 Estimating the performance of activities of daily life

At one month after SCI, the ASIA motor score could explain about 40% of the explained variance of the SCIM total score (see Table 19). Adding age in the model resulted in an improvement of the estimation by about 4%. The negative regression coefficient (-0.256 ± 0.092 (standard error)) indicated that the performance of activities of daily life decreased with increasing age (Table 19). When adding the actual pain level and the pain frequency as a third step in the model, no additional improvement in the explained variance was found, indicating that pain intensity and frequency did not influence the SCIM total score at one month after SCI (Table 19). Similar findings were found when entering average pain and frequency as a third step in the model, but also when adding maximum pain and frequency, the presence of pain or the BDI total score (for the latter one, see Table 20).

Table 19: Motor score, age and pain intensity and frequency as estimates of the performance of daily life activities.

Stage	Predictors	B	Std. Error	R	R2	Adj. R2	Statistical significance (P-value)
1 month	Constant	-3.761	4.442	0.640	0.410	0.404	<.001
	ASIA MS	0.605	0.072				
	Constant	7.257	5.844	0.672	0.452	0.441	.006
	ASIA MS	0.622	0.070				
	Age	-0.256	0.092				
	Constant	8.608	6.319	0.675	0.455	0.433	.768
	ASIA MS	0.629	0.072				
	Age	-0.266	0.095				
	Pain now	-0.310	1.027				
	Pain freq	-0.453	1.348				
3 months	Constant	5.498	4.834	0.725	0.525	0.520	<.001
	ASIA MS	0.763	0.072				
	Constant	29.740	5.477	0.818	0.669	0.662	<.001
	ASIA MS	0.783	0.061				
	Age	-0.542	0.082				
	Constant	28.939	5.801	0.818	0.669	0.656	.900
	ASIA MS	0.785	0.062				
	Age	-0.546	0.084				
	Pain now	0.121	0.952				
	Pain freq	0.334	1.257				
6 months	Constant	7.858	4.505	0.868	0.753	0.749	<.001
	ASIA MS	0.882	0.064				
	Constant	28.671	5.909	0.905	0.818	0.812	<.001
	ASIA MS	0.838	0.056				
	Age	-0.398	0.085				
	Constant	28.898	6.417	0.906	0.821	0.809	.611
	ASIA MS	0.854	0.059				
	Age	-0.406	0.086				
	Pain now	0.832	0.873				
	Pain freq	-1.138	1.330				
12 months	Constant	19.140	7.412	0.833	0.694	0.683	<.001
	ASIA MS	0.792	0.099				
	Constant	30.001	8.338	0.863	0.745	0.726	.028
	ASIA MS	0.853	0.096				
	Age	-0.339	0.146				
	Constant	28.479	8.923	0.869	0.754	0.715	.622
	ASIA MS	0.871	0.101				
	Age	-0.319	0.156				
	Pain now	1.533	1.557				

Abbreviations; B, regression coefficient; Std. Error, Standard error; R, correlation; R2, explained variance; Adj. R2, adjusted explained variance; ASIA MS, motor score according to the American Spinal Injury Association; Pain now, actual level of pain rated on a numerical rating scale (0-10) at the time of assessment; Pain freq, pain frequency (rated as never "0", monthly "1", weekly "2", daily "3" or permanently "4").

Table 20: Motor score, age and depression scores as estimates of the performance of the activities of daily life

Stage	Predictors	B	Std. Error	R	R2	Adj. R2	Statistical significance (P-value)
1 month	Constant	-5.410	5.050	0.643	0.413	0.406	<.001
	ASIA MS	0.627	0.081				
	Constant	6.362	6.765	0.674	0.454	0.441	.014
	ASIA MS	0.625	0.079				
	Age	-0.248	0.098				
	Constant	11.196	7.586	0.683	0.467	0.447	.171
	ASIA MS	0.610	0.079				
	Age	-0.260	0.098				
	BDI	-0.398	0.288				
3 months	Constant	5.102	5.364	0.715	0.512	0.506	<.001
	ASIA MS	0.759	0.080				
	Constant	27.361	6.264	0.796	0.634	0.625	<.001
	ASIA MS	0.770	0.070				
	Age	-0.482	0.090				
	Constant	27.138	6.674	0.796	0.634	0.621	.920
	ASIA MS	0.770	0.070				
	Age	-0.483	0.091				
	BDI	0.034	0.334				
6 months	Constant	8.703	5.345	0.843	0.711	0.705	<.001
	ASIA MS	0.855	0.076				
	Constant	37.242	6.988	0.901	0.811	0.804	<.001
	ASIA MS	0.770	0.064				
	Age	-0.477	0.091				
	Constant	34.812	7.201	0.904	0.817	0.806	0.207
	ASIA MS	0.776	0.064				
	Age	-0.484	0.091				
	BDI	0.383	0.300				
12 months	Constant	19.033	11.554	0.773	0.598	0.576	<.001
	ASIA MS	0.763	0.147				
	Constant	41.245	11.691	0.865	0.749	0.719	.005
	ASIA MS	0.827	0.122				
	Age	-0.569	0.178				
	Constant	54.944	11.950	0.901	0.813	0.777	0.03
	ASIA MS	0.683	0.125				
	Age	-0.414	0.172				
	BDI	-1.123	0.481				

Abbreviations; B, regression coefficient; Std. Error, Standard error; R, correlation; R2, explained variance; Adj. R2, adjusted explained variance; ASIA MS, motor score according to the American Spinal Injury Association; BDI, Beck Depression Inventory.

At three months, similar findings were found (see Tables 19 and 20). The ASIA motor score could explain about 10% more as compared to the condition at one month after SCI, i.e. about 52%. Again, age contributed significantly and increased the explained variance up to 66%. None of the pain intensity and pain frequency combinations, or the BDI total score could significantly contribute to the explained variance of the SCIM total score.

At six months, the ASIA motor score could explain 75% of the SCIM total score. Age increased the explained variance up to 81%. Again, no improvement was found when adding the presence of pain, the pain intensity, pain frequency, or the BDI total scores.

At twelve months, the SCIM total score could be well explained by entering the ASIA motor score (68%) and adding age (73%). While none of the pain factors could significantly contribute to the explained variance (Table 19), the BDI total score significantly increased the explained variance from 72% to 78% (Table 20). For the BDI total score, the negative regression coefficient (-1.123 ± 0.481) indicated that the SCIM total score decreased with increasing BDI score, (i.e. a poorer performance correlated with increased symptoms and attitudes contributing to depression).

3.7 General restrictions on everyday life

When asking the patients how they would score their general restrictions on their everyday life on a scale from 0 (none) to 10 (major restrictions), the average (± standard deviation, SD) scores were 7.4 ± 2.4 (1 month), 6.5 ± 2.5 (3 months), 6.3 ± 2.8 (6 months), and 6.1 ± 2.9 (12 months), showing that patients considered their activities of daily life to be severely compromised. These scores correlated statistical significantly, but only little to moderately with the actual SCIM total scores (at 1 month: r_s = -0.32, P = .001; N = 108; at 3 months: r_s = -0.40, P < .001, N = 102; at 6 months: r_s = -0.48, P < .001, N = 69; and at 12 months: r_s = -0.31, P = .09, N = 31; Figure 11). Interestingly, some persons with no disability in daily life activities (SCIM score ≈ 100) reported considerable interference with daily life activities (NRS = 9). Conversely, some patients reported no interference with daily life activities (NRS = 0), although their SCIM scores were severely reduced (< 10).

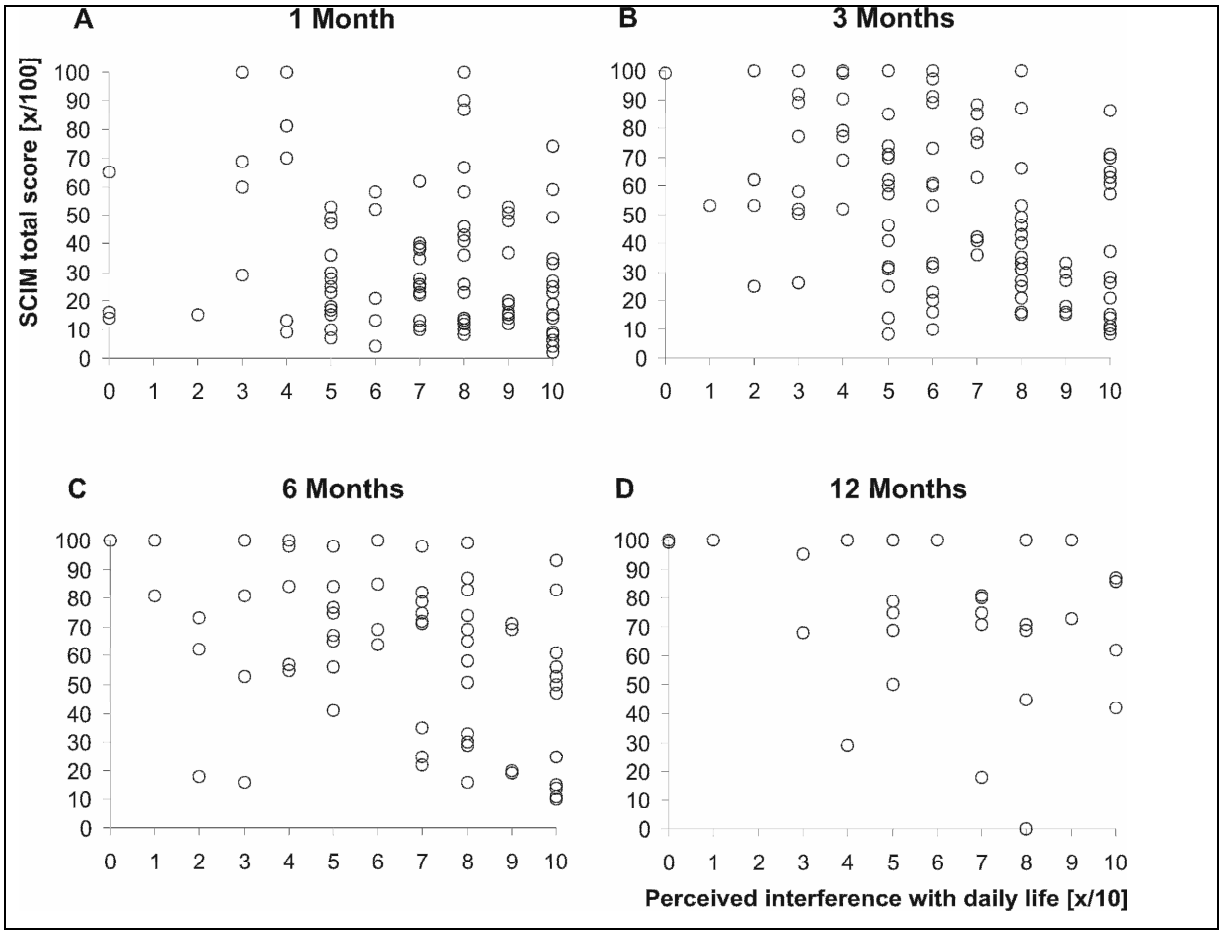

Figure 11: Relationship between perceived interference and objective performance of daily life activities The Spinal Cord Independence Measure (SCIM) score assesses daily life activities and independence. Interference with daily life activities and independence was investigated by asking subjects how they would score the general restrictions on their everyday life on a scale from 0 (none) to 10 (major restrictions). The lack of relationship is evident at all time-points measured after SCI.

Discussion

The aim of this study was to determine whether the occurrence, intensity and frequency of pain, as well as the intensity of a depression have a negative influence on the performance of activities of daily life in persons with SCI, beyond the level of the neurological impairment and age. In the present study, the main findings were the following: (i) the presence of pain, or the intensity and frequency of pain did not relate to the performance of activities of daily life at 1, 3, 6 or 12 months after SCI, (ii) the severity of the depression as measured by the BDI total score contributed significantly to the estimation of daily life performance by about 6% at 12 months after SCI, but was not significant at earlier stages, and (iii) the subjective perception of the SCI persons as

to how their daily life activities were affected by their injury did not correlate significantly to the objective actual level of disability.

Several studies investigated the contribution of factors such as neurological impairment, disability and pain for the quality of life or subjective well-being in persons with SCI (e.g. Abrantes-Pais Fde et al., 2007; Rintala et al., 1998). However, to our knowledge, no study has investigated the influence of pain and depression on functional outcome itself within the first year after SCI.

Initially, the neurological impairment accounted for about 40% of the variance of the performance of daily life activities. This relatively low percentage can be explained by additional factors that influence daily life performance during the early stages of rehabilitation (e.g. initial complications, cardiovascular instability). However, neurological impairment estimated up to 70% of the performance level at 6 months after SCI, which is comparable to a previous study performed in persons two years after SCI (Saboe et al., 1997). At 12 months, this percentage was slightly less.

Besides the motor score, age could additionally account for between 4% and 14% of the performance level of daily life activities. While some studies have found no influence of age on performance and recovery (e.g. Kennedy et al., 2003; Pentland et al., 1995; Yarkony et al., 1988), others have found reduced recovery in older patients (Aito et al., 2007; Scivoletto et al., 1997). In line with these studies, the negative regression coefficient indicated that elderly persons have significantly poorer outcome as compared to younger ones. This was also found in a previous publication analyzing EM-SCI data (van Hedel and Curt, 2006).

The presence of pain, its intensity and frequency, however, did not play a role when estimating daily life performance during the first year after SCI. This is in contrast to many studies that found a negative influence of pain on daily life performance (e.g. (Putzke et al., 2002a; Rintala et al., 1998; Widerstrom-Noga et al., 2001). However, this difference can be explained by several factors. First, the present study was limited to the first year after SCI, while most of the previous studies were performed in community-based samples. One can assume that persons with SCI undergoing rehabilitation are more likely to focus on functional improvement, while psychological and social factors become more important in the domestic environment (Lude et al., 2005). Second, most studies assessed the interference on activities of daily life by

asking, not by assessing, performance of daily life activities (e.g. (Widerstrom-Noga et al., 2001). In the present study, several subjects with a small degree of disability reported a significant amount of interference with their daily life activities and vice versa. Indeed, the relationship between the perception of interference of daily life activities and the actual SCIM scores revealed a poor to moderate correlation. A similar finding was reported previously (Cruz-Almeida et al., 2009) and changes in pain interference status appeared to be unrelated to a change in self-reported handicap (Putzke et al., 2002a). These findings show that perceived interference should not be taken as a measure of actual performance levels, and this has two important consequences: (i) results from previous studies that presumed to have investigated the influence of pain or other factors on daily life activities, but instead assessed the patient's perceived interference rather than an objective performance measure must be interpreted with caution and (ii) discussions centered on selecting the best primary outcome measure for experimental trials (e.g. a phase III trial with the aim to repair or regenerate the spinal lesion (Alexander et al., 2009) must take into consideration that perceived and actual performance can strongly differ. Although the subjective perception of interference (i.e. participation level according to the World Health Organization) might be the most valuable criterion for a patient that would participate in such a trial, it reflects only the subjective interference and not the actual target of such a therapeutic intervention that should be measured by objective parameters (i.e. activity level).

The lack of impact of the severity of the depression on daily life activities during the first six months after SCI could be due to a similar reasoning as to that applied to the findings with respect to pain. Although a SCI is a devastating condition and patients might suffer from negative feelings and grief, depression is not an inevitable consequence following SCI (Kennedy and Rogers, 2000b), and depends rather on available coping strategies of the person with SCI (Lude et al., 2005). One could argue that a depression might occur after being discharged from the rehabilitation center, when patients are confronted with reality, i.e. their disabilities in their own environment. This fits with previous reports on the occurrence of a depression immediately after discharge (Hancock et al., 1993; Richards, 1986). However, our results rather indicate that although a mild to moderate depression could develop during rehabilitation, it is not until after discharge that it affects activities of daily life.

The present results have to be interpreted with respect to the following methodological issues: (i) The SCIM should investigate daily life performance in the person's own environment (Catz et al., 1997). For the in-patient rehabilitation, this environment was the rehabilitation center, which might have influenced the scoring. Although within the EM-SCI network, therapists score, for example, how the patient walks from the room to the therapy location, rather than perform a ten meter walking test, it is a clinical environment that differs from the reality after discharge.

(ii) Although the statistical power needed to detect the influence of pain or depression on performance might require larger sample sizes, we found that the severity of a depression influenced daily life performance at 12 months after SCI, i.e. in the smallest sample.

(iii) Although persons were recruited from several European centers, and therefore are likely to have similar characteristics as the European population of SCI patients, there might be a selection bias due to study inclusion criteria. Some differences compared to general epidemiological numbers (Wyndaele and Wyndaele, 2006) include: (a) age, the SCI persons included in our study were on average about 8 years older, (b) more persons suffered from incomplete lesions (60% versus about 50% in the general population), (c) the samples at 1, 3 and 6 months comprised slightly less tetraplegic subjects than generally observed (about 48% versus 56%) and (d) the origin of the SCI in most subjects in this study was of a traumatic nature (normally about 50%). In addition, we have no information about SCI persons who might have refused to participate, which could have been those with a more severe depression.

(iv) We investigated only the presence, intensity and frequency of the strongest pain, whereas the number of pains experienced, the pain category (nociceptive versus neuropathic) or pain location were not considered. However, the prevalence of pain in our subjects (between 62% and 69%) fits excellently with the mean prevalence of pain in SCI (Siddall et al., 2003).

Conclusions

The present study investigated whether pain and depression influenced the performance of daily life activities in persons within their first year after a SCI. We did not find any influence of pain, while the occurrence of depression influenced activities of daily life performance at one year post-injury. Patients with SCI might be able to cope

with negative syndromes such as pain and depression during initial rehabilitation. However, after discharge, when persons with SCI are confronted with their disabilities in their own daily life environment, a depression could actually affect activities of daily life. Finally, the subjective self-evaluation of the level of interference does not relate well with the objective level of performance of daily life activities. This finding could impact other studies in this field, as well as discussions related to the best primary outcome measures to use in future clinical trials.

4. CONCLUDING REMARK

This thesis focused on the investigation on pain after SCI in a prospective manner. Initially a standardized pain assessment (Pain-Report) was developed, capable of assessing complex pain syndromes and classifying pain types according to the taxonomy of SCI pain (IASP, 2002). A longitudinal study followed, using the Pain-Report with the aims to investigate the incidence and development of pain following SCI. Finally, the influence of pain and depression on activation of daily living was investigated.
Each of the three studies contributed to a better understanding on pain and its impact on daily life tasks in SCI patients.

Pain measurement tools designed for SCI specific pain

Contemporary it is established that pain following spinal cord injury (SCI) is an important issue that often persists and interferes with daily life long after initial injury. When I started with the present thesis no specific assessment tool for SCI patients was established. However, several pain questionnaires investigating neuropathic pain were published i.e. *Neuropathic Pain Symptom Inventory* (NSPI*), Neuropathic Pain Scale* (NPS), *Leeds Assessment of Neuropathic Symptoms and Signs* (LANNS), *Neuropathic Pain Questio*nnaire (NPQ), *Douleur Neuropathique en 4 Questions* (D-4) (for review see Bennett et al., 2007) but none of them was specifically designed for SCI patients. Despite no specific assessment tools clinicians surveyed pain following SCI from single question: *"Do you feel pain?"* to a detailed, long-lasting pain anamnesis. Such variability was leading to inconsistent results that hindered communication among clinicians and researcher as well as the understanding about pain. To achieve evidence based treatment of SCI pain specific pain measurement tools are needed to control for treatment effects. Thus the goal was to fill that gap and to develop a short and precise pain measurement tool specifically for SCI patients that could be applied in both clinical and research fields.
When designing the Pain-Report we followed existing anamnesis instead of a short-form questionnaire. In a questionnaire useful information might not have been captured. In addition, due to the heterogeneity of pain nature and to user-friendliness (e.g. in advantage for tetraplegic patients) we made the decision to use a standardized interview. The Pain-Report consisted further of questions concerning general health, mood, anxiety, sleeping quality, and general physical sequelae of SCI (e.g. muscle

spasm, decreased control of bladder and/or bowel function, infections, ulcers). These items were important to investigate the influence of pain on quality of life and to document possible confounding factors. In 2008 the Pain Data Set (Widerstrom-Noga et al., 2008) was published although without results 90% of the questions were identical to our Pain-Report that showed us to have chosen the right items. In the cross-sectional study the Pain-Report was proven to be feasible and high interrater-reliability in pain classification (using the IASP taxonomy) was achieved.

However, we acknowledge several limitations concerning the classification. At present, no consensus on diagnostic approach to neuropathic pain is agreed and in particular guidelines how to classify pain is lacking. Until this problem is solved screening tools are helpful to identify patients with neuropathic pain (Bennett et al., 2007) and may also be useful in future trials of new therapies (Jensen et al., 2005a). A standardized identification of patients is needed to offer a valid comparison among studies.

Prospective assessment of SCI pain

Despite numerous publications about pain following SCI several methodological problems remained and hindered comparability among researchers. Decades ago numerous studies focused on chronic pain and its course retrospectively. Few have done this prospectively and focusing on the acute stage (e.g. Siddall et al., 1999; Siddall et al., 2003; Jensen et al., 2005b). Several studies investigated if patients differ regarding to pain severity and physiological factors (e.g. level of lesion, completeness of SCI, demographic characteristics) with no satisfying results (Woolsey, 1986; Davidoff et al., 1987; Beric et al., 1988; Richards et al., 1980; Summers et al., 1991; Stormer et al., 1997; Siddall et al., 1999; Werhagen et al., 2004; Aito et al., 2007). No consensus on physical contributors or predictors of pain could be achieved.

To overcome these short-comings, we conducted a prospective study initially focusing on the sub-acute stage (e.g. 4 weeks post injury) and then followed SCI patients over the first 6 months (e.g. using 3 follow-ups). To our knowledge this was the first study that investigated pain after SCI in a European cross-country study by categorizing pain according to the guidelines proposed by the IASP.

With this study we could replicate and confirm the findings of (Siddall et al., 1999) on prevalence of different pain types following SCI. Moreover, we focused on the changing

in pain types according to the defined time points as well as on the shifting between pain types, if any. Since pain displays itself in a heterogeneous manner and its course and intensity might be unpredictable and incalculable we were surprised to find stability in manifestation of the two main pain types (e.g. musculoskeletal and neuropathic pain) within the first 6 months after injury. This finding goes in line with literature about pain in general and supports the observation of clinicians: that once a SCI person develops a pain problem, it is unlikely that pain will vanish on its own (Ehde et al., 2003). Pain can become a life-long experience additional to the burden caused by the injury. Increased pain intensity has been found to be strongly related to negative mood or even depression (Rintala et al., 1998; Krause et al., 2007). A vicious circle might develop: SCI people with increased pain intensities were shown to have poor quality of sleep, as well as high levels of anxiety (Norrbrink Budh et al., 2005); both are related to a decreased pain threshold. Since pain is mostly perceived as a negative and unpleasant stimulus it is not surprising that high levels of pain are related to depressive mood and to a reduced wellbeing. The ongoing longitudinal study will reveal, whether these findings are also shown in our sample. In addition, the fact that the same pain persists over 6 months we are interested to see whether the stability persists over a longer time.

The influence of pain on daily living

Since the Pain-Report is incorporated into a setting that investigates various consequences after SCI multiple correlation were computed with results from other assessments tools. Especially functional assessments were used to investigate the impact of pain on the functional outcome after SCI.

It is generally agreed that pain and / or the severity of depression can interfere with the rehabilitation outcome (Budh and Osteraker, 2007; Middleton et al., 2007; Putzke et al., 2002b; Westgren and Levi, 1998; Hammell, 2007; MacDonald et al., 1987; Malec and Neimeyer, 1983). However, there are some methodological limitations since most studies investigated community-based samples and the subjective interference rated by patients instead of assessing the objective level of performance.

Unexpectedly, the presence of pain, or the intensity and frequency of pain did not relate to the performance of activities of daily life up to 12 months after SCI. Findings

concerning depression revealed that although a depression might occur within the first 6 months a negative influence on daily activities could have been shown latest at one year post injury. One reasonable explanation might be that after discharge the patient starts to realize his limitations; with this confrontation frustration is increasing. Being frustrated includes unpleasant feelings this in turn can lead to a depressive mood. Furthermore, the subjective perception of the SCI patient did not correlate significantly to the objective actual level of disability. Since patients with a small degree of disability reported a high interference (10 on a NRS) with their daily life activities and vice versa. This fact demonstrates how different clinical staff and patient might regard the situation. This might give an explanation for the contrast in findings from other studies which are reporting about a negative influence of pain on the rehabilitation outcome (Putzke et al., 2002b; Rintala et al., 1998; Widerstrom-Noga et al., 2001). In addition, we have investigated the sub-acute phase after injury while other studies evaluated community-based samples.

Pain and its psychosocial components

A significant minority of people with SCI is at higher risk to develop several psychological morbidities: several studies suggest an increased level of anxiety in SCI subjects, ranging from 13% to 30% (Craig et al., 1994; Scivoletto et al., 1997; Kennedy and Rogers, 2000a). Similar rates are reported for PTSD symptoms (North, 1999) ranging between 14% (Kennedy and Evans, 2001) and 44% (Chung et al., 2006).
Stormer et al. (1997) found that the only factor which is related to pain severity is depressed mood. Pain no matter what origin might be aggravated and maintained by psychological mechanisms (Widerstrom-Noga and Turk, 2003). Therefore, one can conclude that SCI pain might be related to adjustment problems.
Perception of pain includes an extreme distress in patients. Mostly, mediated by a number of factors of a person's belief or sense of self-confidence like perceived control, learned helplessness or self-efficacy, and coping styles. Craig et al. (1994) suggested that up to 40% of people with SCI have more external perceptions of control, lower levels of self-esteem and more helpless and fatalistic coping strategies compared to able-bodied controls one year after injury. More, the likelihood of experiencing a PTSD, increased pain intensity as well as general health problems is related to having an

external locus of control (Chung et al., 2006; Wollaars et al., 2007). Norrbrink Budh and Lundeberg, (2005) investigated predictors for the use of analgesic drugs and found that not the intensity of pain was predictive for the use of analgesics but pain unpleasantness. This suggests that the appraisal of pain perception is in the foreground and influences strongly the patient's action.

However, it could be demonstrated that experiencing pain is inseparable to the individual's perception and appraisal and that we should not underestimate the power of the mind and its ability to modulate pain.

Approaching a successful treatment of pain after SCI

Several studies investigated treatments, which are used by SCI pain patients, and their effectiveness: Commonly used treatments can be grouped in following categories, such as pharmacological approaches, surgical approaches, psychosocial modalities, electrical stimulation procedures, neurolytic injections, and physical modalities, additionally in some studies are also alternative treatments mentioned (Warms et al., 2002; Widerstrom-Noga and Turk, 2003).

Warms et al. (2002) investigated this treatments and their influence in pain relief in a community-based SCI sample (n= 471) with the following results. The most common applied treatments were medication, especially NSAID's, acetaminophen, and opiods, used by more than 50%. Most commonly used non-pharmacological treatment was physical therapy, which was used by 68%. Interestingly, treatments used most often are not the ones which are also the most helpful ones; as none of the patients reported to have a complete pain relief. For example, the most helpful rated treatment was opiod medication (mean 3.47 ± 1.22, rating scale 1= not at all helpful to 5= extremely helpful) demonstrating that opioid was only partially pain relieving. Similar results were found by (Widerstrom-Noga and Turk, 2003) where the perceived most effective treatment was again physical therapy and medication like opioids and anticonvulsants but only one third of those who took them reported pain relief. Again, this study could show that the intake of some medication is strongly related on the individual's perception, respectively appraisal of pain.

Regular exercise or physical activity is rated as very helpful, although investigated only in small number of patients. Among nine SCI persons who reported about physical

activity, seven rated it as extremely helpful and pain relieving (mean 4.75 ± 0.50) (Warms et al., 2002).

Based on these results the author's suggest that pain should be treated by increasing exercises. Physical therapy/activity combines numerous factors like movement, diversion, being focused on one thing, and experiencing feeling of reward afterwards. Since pain is not a single entity it is not adequate to treat it like one (for example medication is a unidirectional approach). This approach goes in line with the definition of pain (see chapter 1), which emphasizes the complexity and multidimensionality of pain.

Further, it is suggested that the optimal treatments should target all underlying pathophysiology and contributing psychosocial factors. In addition, it reflects the difficulty in translating findings based in animals into treatments for human and points out the importance of focusing on the individual's perception / appraisal of pain.

Therefore, since conventional pharmacological treatments fail to decrease pain intensity the most efficient treatments at present are those of psychological nature. These findings argue for using psychological treatment strategies, which might influence the affective-motivational component of pain (see chapter 1.3.1.), anxiety, depression and quality of life. Thus, the heterogeneity of pain may not only be a disadvantage and since pain is composed of several components we might influence at least one of the components.

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APPENDIX

Schmerz-Protokoll

Anleitung für die Schmerzbefragung

Die Fragen sind nummeriert und sollten in dieser Reihenfolge abgehandelt werden. ***Fett*** *gedruckt sind mögliche Frageformulierungen. Mehrfachantworten sind bei den meisten Fragen möglich. Alle Fragen betreffen die letzten 7 Tage vor dem Interview.*

Patient: ……

Datum: …….. Messzeitpunkt: 1 / 2 / 3 / 4

Klassifikations-Code:……...../……../……...

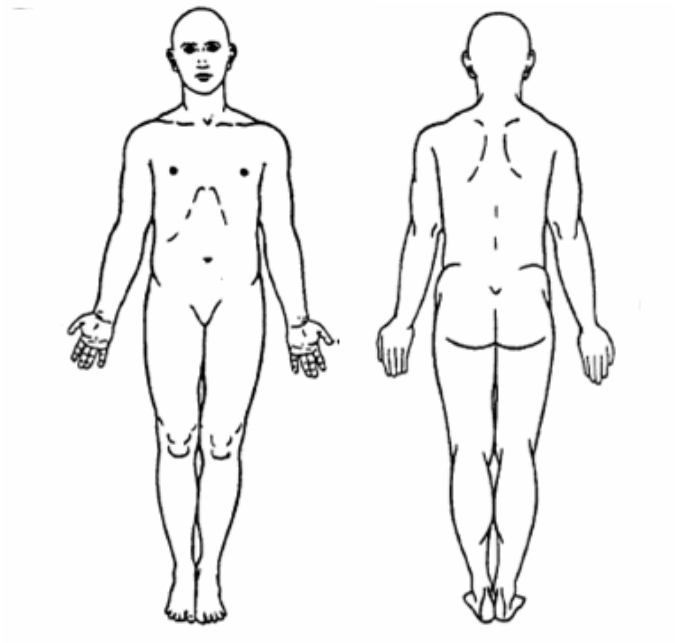
1. Haben Sie Schmerzen? J / N

Falls **„Nein"** bitte mit den Fragen zum allgemeinen Gesundheitszustand (17-23) fortfahren!

2a. Hatten Sie diese Art von Schmerzen bereits vor dem Unfall? J / N
2b. Hatten Sie chronische Schmerzen irgendeiner Art? J / N
3. Hatten Sie vor dem Unfall depressive Episoden? J / N

4. Nehmen Sie Medikamente einer der hier genannten Stoffgruppen ein? *(bzw.nachsehen in Akte)*
□ NSAR (u.a periph.) Analgetika: ……
□ Antidepressiva: ……..
□ Antiepileptika: ……
□ Opioide: ……..
□ Spasmolytika: ……
□ Hypnotika (Tranquilizer): ……
□ Drogen / Alkoholabusus: ……
□ Neuroleptika……..
□ Andere……...
□ Keine

5. Piktogramm: Wo sind die Schmerzen lokalisiert*?*
Möglichst genau auf dem Körperschema einzeichnen. Falls mehr als ein Schmerztyp vorhanden ist, bitte diese der Wichtigkeit nach nummerieren und jeden Schmerz einzeln befragen!



Schmerz 1

6. Wie würden sie ihren Schmerz beschreiben? Treffen die folgenden Beschreibungen auf ihren Schmerz zu? In welcher Intensität? *Die häufigsten Beschreibungen der jeweiligen Schmerzqualitäten sind erwähnt, sollten diese zutreffen, diese in der vorkommenden Intensität ankreuzen. Zusätzliche Beschreibungen können unter Bemerkungen notiert werden.*

		überhaupt nicht	**kaum**	**gering**	**stark**	**sehr stark**
A	bewegungsabhängig	□	□	□	□	□
	lokalisiert	□	□	□	□	□
	klopfend	□	□	□	□	□
B	krampfartig	□	□	□	□	□
	dumpf	□	□	□	□	□
	wellenförmig	□	□	□	□	□
	im Bauch lokalisiert	□	□	□	□	□
C	brennend	□	□	□	□	□
	stechend	□	□	□	□	□
	kribbelnd	□	□	□	□	□
	einschiessend	□	□	□	□	□

7. Allodynie: Kann im schmerzhaften Gebiet z.B. schon eine leichte Berührung schmerzhaft sein? *(Bsp.: Haut kann empfindlich sein wie bei einem Sonnenbrand)*

□ □ □ □ □

8. Parästhesie: Kennen sie Empfindungen, wie z.B. Kribbeln, Taubheit, Kälte- oder Wärmewahrnehmungsstörungen, die entweder durch Berührung ausgelöst werden oder spontan auftreten?

□ □ □ □ □

9. Wie intensiv /stark / unerträglich sind die Schmerzen auf einer Skala von 0-10? 0 = keine Schmerzen – 10 = stärkste Schmerzen, die sie sich vorstellen können.

9a. Im Moment? ……..
9a*. Durchschnittlich in den letzten 7 Tagen?* ……..
9b*. Und wie stark sind die maximalen Schmerzen?* ……..

10. Wann haben sie diesen Schmerz das erste Mal verspürt?
□ Innerhalb der ersten 2 Wochen
□ Innerhalb des ersten Monats
□ 1-3 Monate nach der Verletzung
□ 3-6 Monate nach Verletzung
□ 6-12 Monate nach Verletzung
□ Nach 12 Monaten und länger

11. Wie häufig spüren sie den Schmerz?
□ Dauerschmerzen
□ Täglich
□ Wöchentlich
□ Monatlich

12. Gibt es einen Tagesverlauf des Schmerzes?
□ Morgens maximal
□ Mittags maximal
□ Abends maximal
□ Nachts
□ Kein Tagessverlauf

13. Hat sich der Schmerz mit der Zeit verändert?
□ Keine Veränderung
□ stärker als zu Beginn
□ schwächer als zu Beginn

14. Treten im Zusammenhang mit Schmerzen folgende Begleiterscheinungen auf?

Übelkeit	J / N
Schwitzen	J / N
Herzrasen	J / N
Kopfschmerzen	J / N

15. Kennen Sie Faktoren, die ihren Schmerz lindern? *Falls einige zutreffen bitte umkreisen.*
Temperaturwechsel – emotionale Faktoren
Lagewechsel– Bewegung – Medikamente - Alkohol – Andere – Keine

16. Kennen sie Faktoren, die ihren Schmerz auslösen oder verstärken?
Temperaturwechsel – psychischer Stress – Entspannung – Berührung– Spastik – Blasenprobleme – Verstopfung – veg. Symptome - körperliche Belastung – Andere- keine

<u>Nun würde ich gerne ein paar Fragen zu Ihrem allgemeinen Zustand stellen:</u>
Die Fragen beziehen sich auf die letzten 7 Tage.

17. Wie ist der Antrieb, die Motivation?
Der Antrieb beruht meist auf einer Fremdeinschätzung
□ normal
□ reduziert
□ gesteigert

18. Wie würden Sie Ihren allgemeinen Gesundheitszustand einschätzen?
□ Sehr gut
□ Gut
□ Zufrieden stellend
□ Schlecht
□ Sehr schlecht

19. Wie würden Sie Ihre allgemeine Stimmung auf einer Skala von 0 bis 10 einschätzen?
0 sehr schlecht 10 sehr gut……

20. Wie würden Sie Ihre allgemeine Ängstlichkeit auf einer Skala von 0 bis 10 einstufen?
0 keine Angst 10 sehr ängstlich……..

21. Wie würden sie ihre Schlafqualität auf einer Skala von 0 bis 10 einstufen?
0 Schlaflosigkeit 10 ungestört ……

22. Wie würden sie ihre generelle Einschränkung im Alltag auf einer Skala von 0-10 einstufen?
0 keine 10 starke Einschränkung……

23. Nun möchte ich noch einige typische Begleiterscheinungen, die mit dem Krankheitsbild einhergehen, erfragen. Ich werde diese der Reihe nach erwähnen und ich bitte Sie, falls Sie diese Begleiterscheinung kennen, mir ihre subjektiv empfundene Beeinträchtigung dadurch auf einer Skala von 0 bis 10 wiederzugeben. *(O = überhaupt nicht stark; 10 = sehr stark)*

□ Muskelspasmen……..

□ verminderte Kontrollfähigkeit der Blase……...

□ verminderte Kontrollfähigkeit der Darmtätigkeit……

□ Infektionen……

□ Schmerz……

□ Druckstellen……

□ verminderte Sexualfunktion……

□ verminderte Fähigkeit zu gehen oder sich zu bewegen……..……....

□ soziale Aktivitäten……